

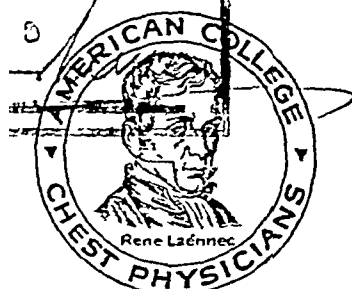


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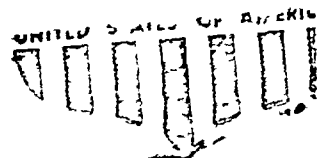
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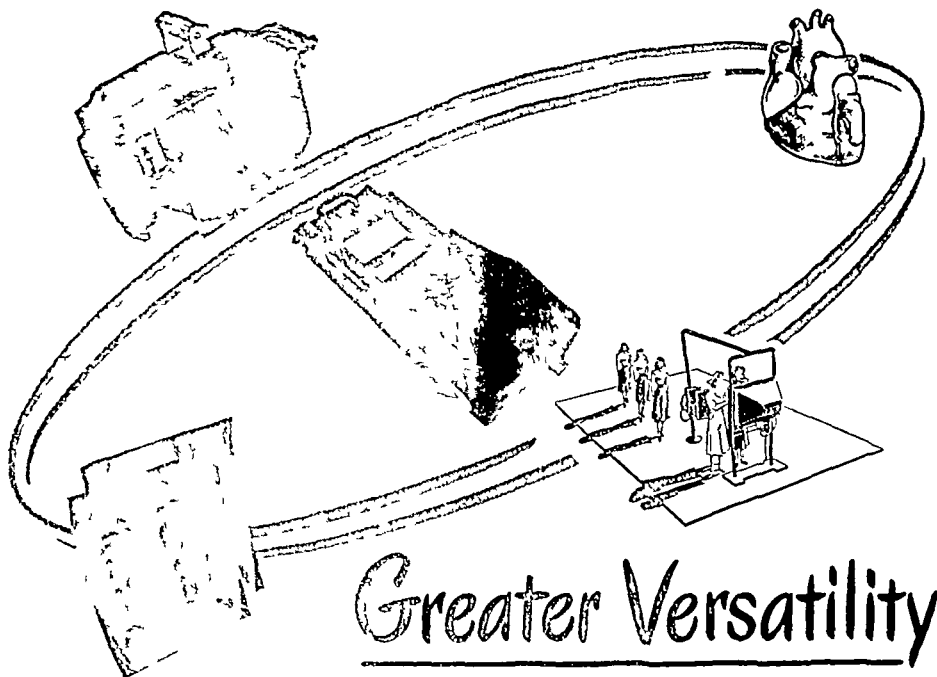
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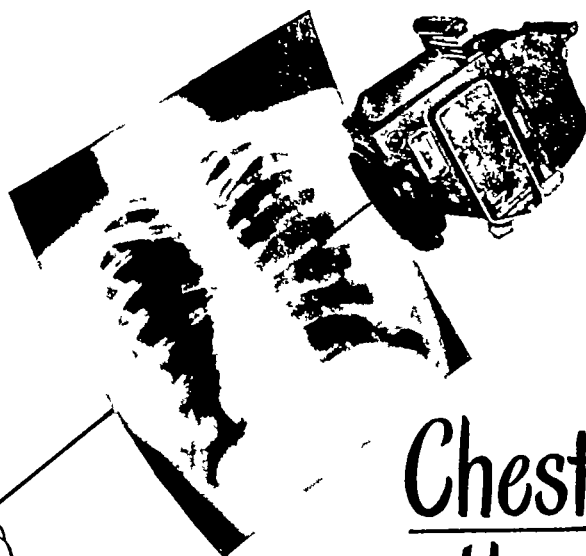
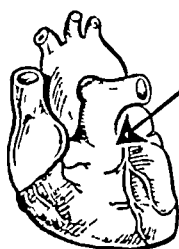
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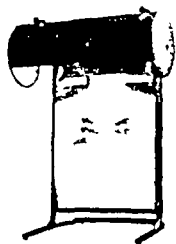
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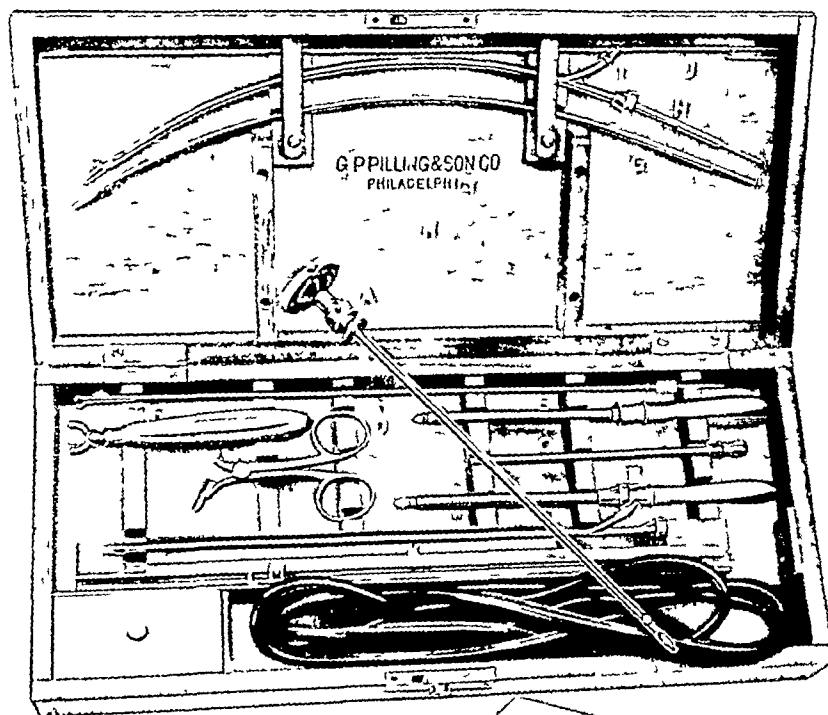
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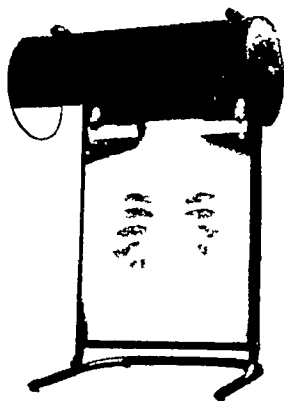
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## Postmortem Pneumothorax\*

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If the thorax of a cadaver is opened, or if a hypodermic needle is inserted post mortem through the chest wall into the pleural cavity, there is produced a small pneumothorax space. The room air enters the pleural cavity until the intrapleural pressure becomes atmospheric. The size of the space so produced depends chiefly upon the degree of retractility of the lung, and secondarily upon such factors as the nature of the disease in the lung, the degree of subatmospheric pressure in the pleural space, the presence of pleural adhesions, the mobility of the chest cage, and the length of time after death. Under the most favorable conditions the pneumothorax occupies from 5 per cent to 15 per cent of the pleural cavity.

We have increased the size of this pneumothorax by pumping air under pressure into the pleural cavity. Large pneumothorax spaces were thus produced and a variety of pulmonary collapses obtained. Of course, such a positive pressure pneumothorax over a dead and partially inelastic lung cannot be compared too closely with a subatmospheric pneumothorax over a living lung, but many of the effects are so similar and even identical that it stresses the importance of the strictly mechanical factors involved in pneumothorax.

### *Technique*

Shortly after death, from a few minutes up to three hours, the cadaver was brought to the x-ray room and seated in a specially constructed chair mounted on wheels and having a cassette holder in its back.<sup>1</sup> Our room was so arranged that the cadaver could be

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placed in front of the upright fluoroscope or the regular x-ray tube to permit fluoroscopy and the taking of a six-foot film without disturbing the position of the chair or the cadaver

A six-foot film was made of the thorax prior to any procedure. Then, under fluoroscopic guidance, a 16-gauge needle was inserted through the chest wall into the pleural cavity. The needle was attached to a Potain aspirator and air was pumped into the pleural cavity. The pneumothorax so produced was followed under constant fluoroscopic vision. The pressure used was often considerable and was measured by an attached manometer. Air was forced into the pleural cavity until the lung ceased to collapse. At this point of maximum collapse there was usually an escape of pleural air around the needle into the muscle planes and subcutaneous tissue (Figures 3, 5, 8, 17)

The final intrapleural pressure (after the maximum pulmonary collapse) ranged from atmospheric to 30 cm water. The lung remained small, but its size could be altered by either withdrawing some of the pleural air or by producing a contralateral pneumothorax. If even a slight amount of air was withdrawn the intrapleural pressure became subatmospheric and so remained.

In this study, pneumothorax was produced from several minutes to three hours after death, in bodies still warm, in some that were at room temperature, and in others in complete rigor. The degree and type of pulmonary collapse was not materially altered by these factors during this time interval.

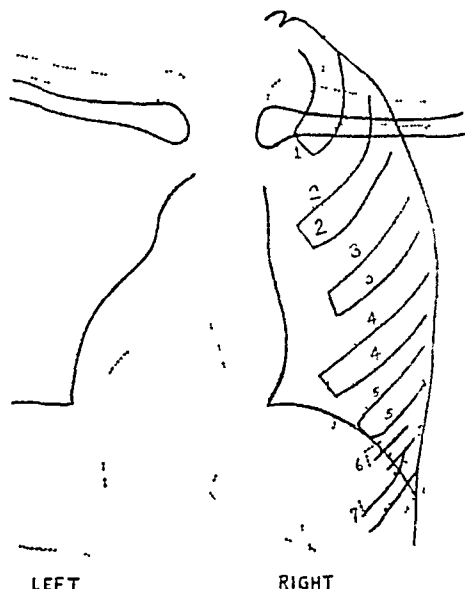


FIGURE 1

Effect of a postmortem pneumothorax on the motion of the bony thorax. The solid line shows the ribs, clavicle, heart and diaphragm prior to the pneumothorax. The dotted line shows them and the right lung after a bilateral collapse.

### *Material*

This study was begun in 1937 and ended in 1941. A total of 80 cadavers was used. The chief pulmonary lesion was cavernous tuberculosis in 74 cases, miliary tuberculosis in 2 cases, emphysema in 2 cases, silicosis in one case, and bronchiogenic carcinoma in one case. From a total of 160 sides, some degree of pneumothorax was obtained in 119 (or 74 per cent). The other 41 sides showed complete obliteration of the pleural space. Necropsies were done in 34 cases (or 42 per cent).

The results obtained will be discussed in sections dealing with the effects of the pneumothorax upon the bony thorax, diaphragm, heart, anterior mediastinum, lungs, and pleural cavities. The effects of aspiration of air from pulmonary cavities will also be mentioned. In general, all these structures were profoundly affected and showed many changes similar to those seen with pneumothorax in the living patient.

### *Bony Thorax*

In both uniform and irregular pneumothoraces the ribs were elevated and became more horizontal. This movement upward was greatest in the lower ribs anteriorly and least in the upper ribs posteriorly. The movement upward measured from 1 to 3 cm anteriorly. The interspaces were widened, especially the lower ones, and the sternum and clavicles were also elevated though



FIGURE 2

FIGURE 3

Figure 2 Case 7 Postmortem film prior to pneumothorax. The right apex shows good aeration—Figure 3 Case 7 Right pneumothorax with atelectasis in upper lobe selective collapse air in soft tissues and displacement of the heart



to a lesser degree than the ribs. The width of the hemithorax with the air space showed an increase in size by about 2 cm. The effects were similar to those seen with pneumothorax in the living (Fig 1)

### *Diaphragm*

During the induction of the pneumothorax the hemidiaphragm moved downward and continued to do so until a maximum pulmonary collapse was obtained. The descent was very slight with small and irregular pneumothoraces, but reached from 4 to 10 cm in large collapses. A small basal pneumothorax produced a greater descent than a large apical one. Each diaphragmatic leaf moved independently of the other and maintained its dome-shaped contour. Despite the many poor collapses in this series an appreciable descent occurred in 95 sides, or 80 per cent (Figs 5, 7, 8, 12, 14)

### *Heart*

In this group of 119 pneumothoraces the heart and large vessels were fixed and immobile in 30 cases and freely movable in 89 cases (or 75 per cent). In all cases the prepneumothorax picture was typically cadaveric—wide heart and vessel shadows and a small longitudinal diameter. The cases showing a mobile heart presented some degree of movement in two directions. The heart

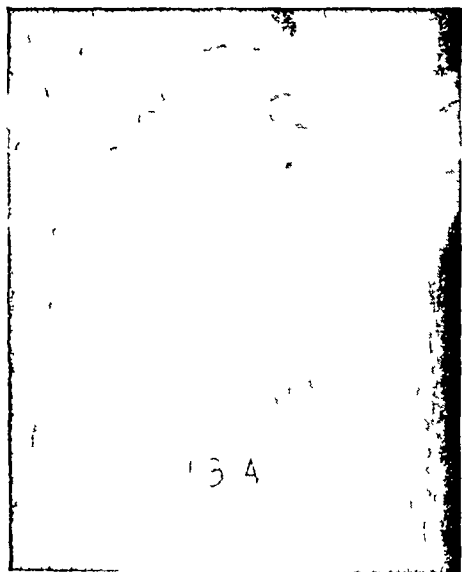


FIGURE 4



FIGURE 5

*Figure 4, Case 13* Postmortem film prior to pneumothorax. The left lung is completely excavated; the right lung shows two large cavities—*Figure 5, Case 13* Right pneumothorax. Note the "airlessness" in the upper two-thirds of the right lung, the obscuration and small size of the two large cavities, the descent of the right hemidiaphragm, the cardiac displacement, and some intrapleural fluid.

and vessels were lengthened (sometimes considerably) and the transverse diameter was decreased. The antero-posterior diameter was increased so that the heart was flatter when viewed from the side and occupied more space posteriorly. The effect of these two movements presented a heart which was lengthened from its base to its apex, flattened, and showed some increase in size posteriorly.

A right pneumothorax displaced the heart to the left. The shift was often considerable and reached 6 to 8 cm. The right border of the heart was often not seen because of its displacement. A left pneumothorax displaced the heart similarly to the right. A unilateral pneumothorax produced little or no lengthening of the heart. In bilateral pneumothorax the heart was first displaced to one side and then back to the midline by the second pneumothorax, and its final picture showed it to be longer and narrower than before. Only a bilateral pneumothorax and a bilateral descent of the hemidiaphragms produced much lengthening of the heart. In such cases the heart assumed the typical picture seen in advanced emphysema in the living—long and narrow with often a prominent pulmonary conus.

In several cases of right-sided pneumothorax the first displacement of the heart occurred in the upper left border producing a bulge and a deformity similar to that seen in mitral stenosis (Figs 1, 3, 5, 7, 8, 10, 12, 14, 17).

#### *Anterior Mediastinal Hernia*

A pleural anterior transmediastinal hernia occurred in some degree in a large number of the pneumothoraces but was especially marked in 16 cases. The mesial pleural reflection and the contained pleural air was easily followed fluoroscopically across the midline to the other side. These 16 cases showed a pleural shift of 2 to 6 cm. past the mid-sternal line and the herniation grew larger as the pneumothorax was increased. The hernial space extended from the first rib to the fourth and often to the fifth. In three cases, as the pneumothorax was increased, the greatest width of the herniation moved upward from the level of the fourth rib to that of the third.

The herniation was usually made smaller by a contralateral pneumothorax and, in cases of uniform bilateral collapse, was entirely abolished. Several cases showed small posterior mediastinal hernias (Figs 7, 8, 13, 14).

#### *Type of Pulmonary Collapse*

A unilateral pneumothorax was obtained in 41 cases and a bilateral one in 39 cases resulting in 119 spaces. In 9 spaces the collapse

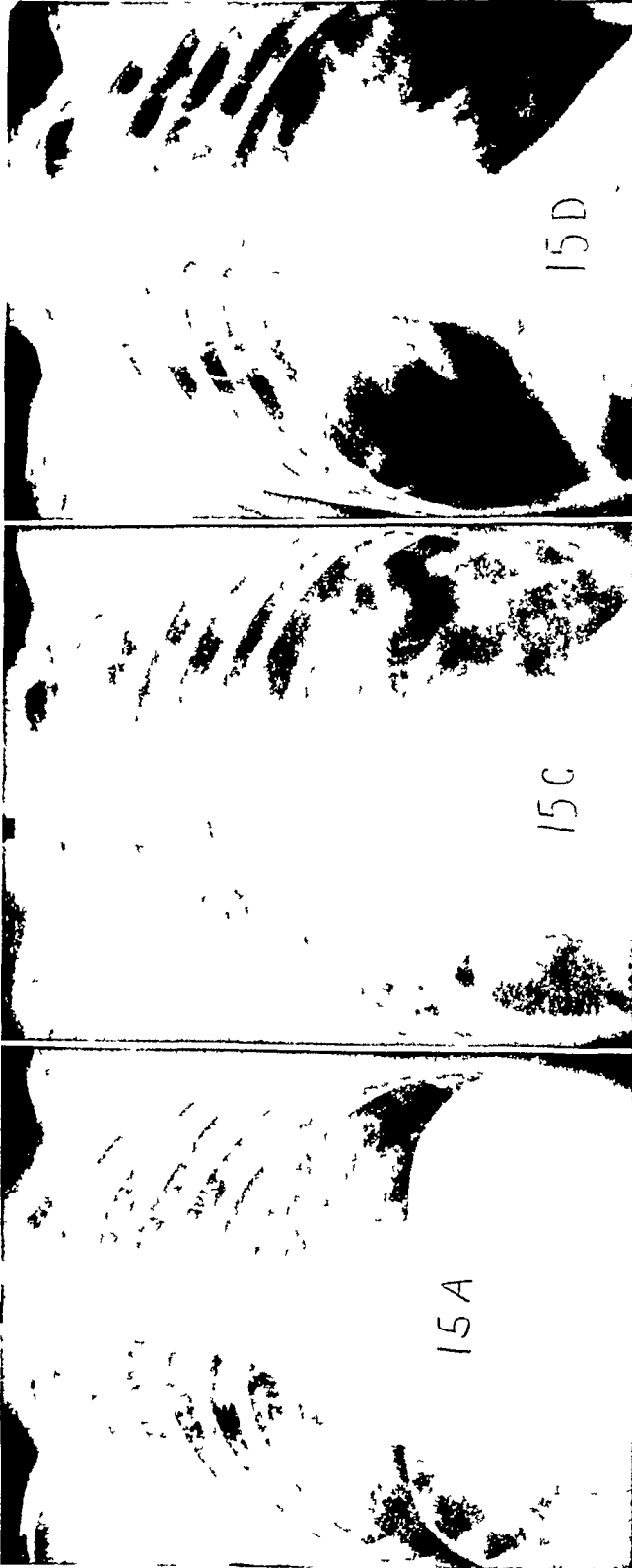


FIGURE 6

FIGURE 7

FIGURE 8

Figure 6, Case 15 Postmortem film prior to pneumothorax—Figure 7, Case 15 Right pneumothorax Note the depression of the right hemidiaphragm, displaced heart, anterior mediastinal hernia, distortion of the pulmonary cavity—Figure 8, Case 15 Bilateral pneumothorax Note the low diaphragm, cardiac position and contour, abolition of the hernia

was small, localized, and insignificant. In 76 spaces the pneumothorax was modified greatly by pleuro-pulmonary adhesions and presented all degrees and types of collapse. In 34 sides the air was quite uniformly distributed over the entire lung, 10 of these showed a moderate number of adhesions which apparently prevented a better local collapse, and 24 showed a more ideal collapse involving the entire lung and not affected by the few fine adhesions seen.

The 34 sides mentioned showed collapses varying from 20 to 80 per cent with an average collapse of 50 per cent for the group. One lung showed a 20 per cent collapse, 5 lungs a 20 to 30 per cent collapse, 9 lungs showed 30 to 40 per cent, 11 lungs showed 50 per cent, 3 lungs 60 per cent, 2 lungs 70 per cent, and 3 lungs 80 per cent.

The 76 sides mentioned above presented irregular collapses varying from a relatively small volume to over 50 per cent. Thus 50 lungs showed a collapse under 30 per cent, 22 lungs from 30 to 50 per cent, and 4 lungs over 50 per cent.

#### *Pneumothorax in a Free Pleural Space*

The 24 sides with the more ideal collapse showed very few or no adhesions roentgenologically. The collapse obtained varied from 30 to 80 per cent with a mean average of 55 per cent. This group included 20 cases of ulcerative or exudative tuberculosis, 2 cases of miliary tuberculosis, 1 case of bronchiogenic carcinoma with emphysema, and 1 case of emphysema with myocardial failure.

Necropsies were done in 12 cases of this group and the adhesions noted. One case showed no adhesions at all, 7 cases showed only a few slight strands, and 4 cases a moderate number of long, string-like adhesions. None appeared to influence the degree of collapse as all were fine, long, and not under any tension. The case without any adhesions showed a collapse of 80 per cent, the 7 cases with the few strands showed a mean collapse of 53 per cent (40, 40, 40, 50, 60, 70, 70 per cent) and the 4 cases with more adhesions showed an average collapse of 52 per cent (40, 50, 50, 70 per cent).

The degree of pulmonary *infiltration* or the amount of disease present was divided roughly as mild, moderate, and extensive. Nine cases with a mild amount of disease showed an average collapse of 60 per cent. Six cases with a moderate amount showed an average collapse of 50 per cent, of this number there were three with localized disease and a collapse of 60 per cent, and three with uniformly scattered disease and a collapse of 40 per cent. Nine cases with extensive disease averaged 45 per cent collapse and, of this number, five with localized disease and four

with disseminated disease showed the same degree of collapse

The degree of pulmonary *cavitation* and the degree of maximum collapse were correlated. Eleven lungs had no cavities and showed an average collapse of 60 per cent, eight lungs had cavities up to 4 cm and showed a collapse of 50 per cent, two lungs with cavities from 4 to 6 cm showed a collapse of 40 per cent, and three lungs with cavities over 6 cm showed a mean collapse of 35 per cent.

The amount of *normal lung tissue* appeared to be a factor. Seven lungs showed only a slight amount of normal tissue and presented an average collapse of 45 per cent, six cases with a moderate amount of normal tissue showed a 45 per cent collapse, eight cases with a large amount of normal tissue showed a 70 per cent collapse. Three cases with emphysema showed a 55 per cent collapse.

In summary, (1) the greater the amount of pulmonary disease the less was the degree of collapse obtained in an essentially free pleural space, (2) the greater the degree of cavitation, the less was the collapse, (3) the more normal lung tissue present, the greater was the collapse, and (4) the three cases of emphysema showed less collapse than those with a similar amount of normal tissue. Therefore, one may expect the best pneumothorax collapse in instances showing a small amount of disease, a small cavity or none at all, a large amount of normal alveolar tissue, and no emphysema.

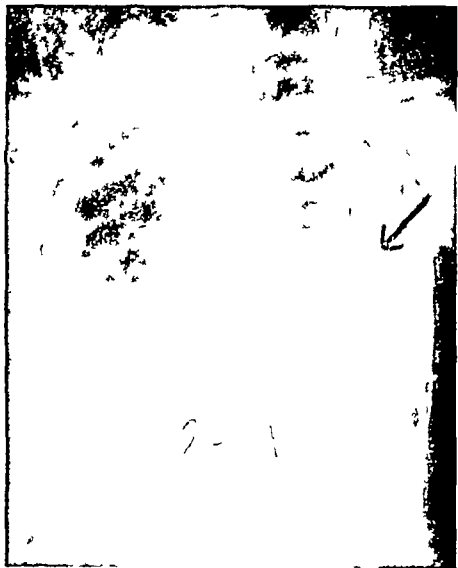


FIGURE 9

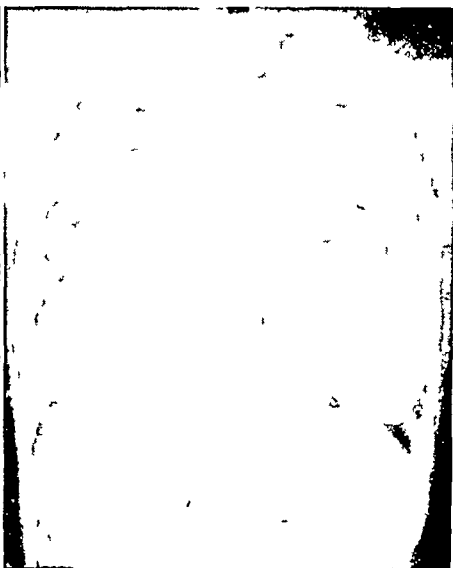


FIGURE 10

*Figure 9, Case 24* Prior to pneumothorax. The left lung is completely excavated, the right lung shows a large apical cavity and a smaller one below it. *Figure 10, Case 24* Right pneumothorax. The small cavity is "closed" and the large one is smaller and shows a greater fluid level. Note also the cardiac displacement and its effect on the fluid level in the left-sided cavity.

### *Selective Collapse*

A total of 14 pneumothoraces showed selective collapse, 10 at the apex and 4 at the base. Seven of this group were associated with a relatively free pleural space and 7 had gross adhesions which did not prevent the collapse. The diseased apical portion was seen fluoroscopically to undergo collapse first after the injection of only a small amount of air, the rest of the lung then followed. Two of these cases were associated with premortem lobar atelectasis (Figs 3, 13, 17).

Four of these cases were necropsied. One showed extensive caseous pneumonia with small islets of normal tissue, little liquefaction, and normal bronchi grossly. The second showed extensive confluent caseous masses and normal bronchi. The third also showed confluent caseous masses, normal bronchi, and no gross cavitation. The fourth showed numerous exudative areas at the base and the bronchi were normal.

The ten cases not necropsied showed the following prepneumothorax roentgen pictures:

- (1) dense exudative lesions in entire lung and chiefly in the lower lobe,
- (2) dense exudative areas chiefly in the upper lobe (Figs 2, 3),
- (3) moderately dense productive nodules chiefly in the upper lobe,
- (4) contracted, atelectatic, excavated, and fibroid upper lobe,
- (5) (6) bilateral, fine, symmetrical miliary tuberculosis (Figs 11, 13),
- (7) moderately dense productive lesions in the right lower lobe with a 6 cm cavity at the apex of this lobe,
- (8) moderately dense infiltration chiefly in the upper lobe with a 3 cm apical cavity,
- (9) light exudative infiltration in the upper lobe,
- (10) dense confluent bronchopneumonic areas at base and normal bronchi (Figs 16, 17).

It is to be noted that 8 of these lungs showed extensive disease in the selectively collapsed lobe, 1 had a miliary tuberculosis, and 1 had a light infiltration.

### *Atelectasis*

The term atelectasis is used to denote airlessness which occurred only in a lobar distribution in this group of cases. Six such cases were noted and two of them were present prior to the pneumothorax. The right upper lobe was involved four times, the right lower lobe once, and the left lower lobe once. Only one case was necropsied. A description of each case follows.

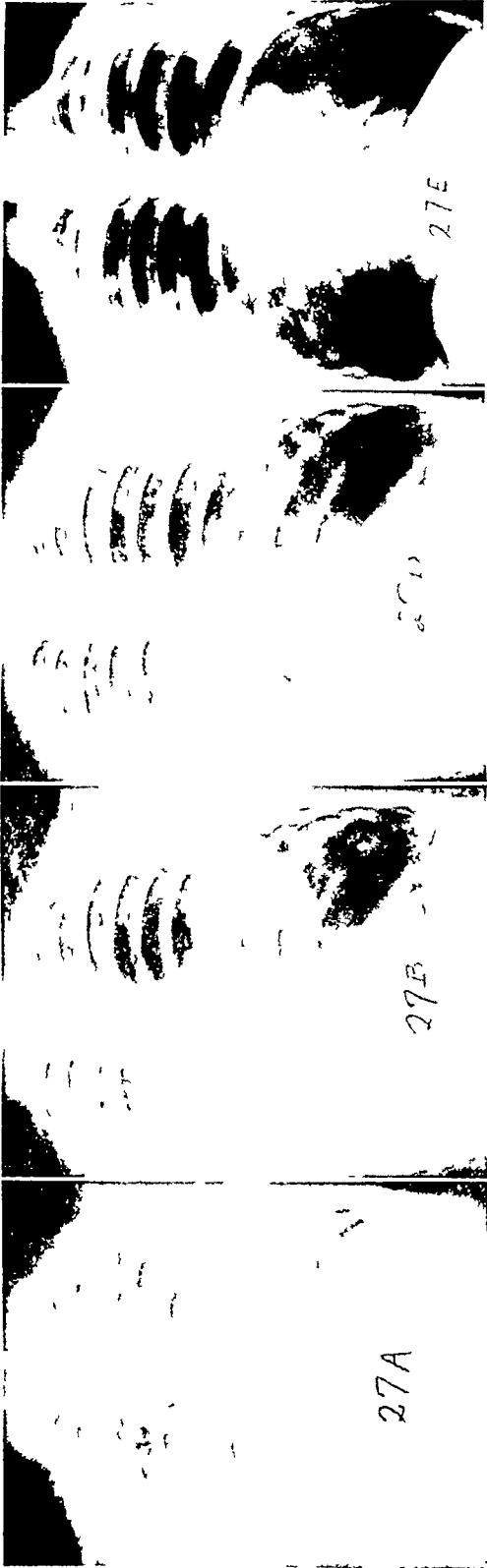


FIGURE 11

FIGURE 12

FIGURE 13

FIGURE 14

Figure 11, Case 27 Postmortem film showing a fine miliary disseminated infiltration—Figure 12, Case 27 Right pneumothorax showing a large pulmonary collapse low hemidiaphragm, displaced heart, and anterior hernia—Figure 13, Case 27 Left pneumothorax Note collapse of the upper lobe only—Figure 14, Case 27 Left pneumothorax continued Note the pulmonary collapse, low diaphragm, shape and position of the heart, absence of the hernia, and change in shape of the bony thorax

*Case 1* (Figs 2, 3) Prior to collapse the x-ray film showed a dense exudative lesion in the entire lung especially marked at the right sub-apex. After the pneumothorax the lobe showed a selective collapse and the rest of the lung an ordinary one. The previously aerated apex became a dense homogeneous shadow. A bronchogram was then made with a barium emulsion and it showed poor filling of the larger bronchi and none of the smaller ones. Prior to the pneumothorax the post-mortem intrapleural pressures were  $-13$  cm water over the upper lobe and  $-5$  cm over the lower lobe.

*Case 2* (Figs 4, 5) The x-ray film showed a series of cavities occupying two-thirds of the entire lung field and measuring  $17$  cm, and a dense homogeneous shadow laterally over the right upper lobe. After pneumothorax the upper two-thirds of the lung showed a dense homogeneous 'airless' picture through which rarefactions could be seen and the lower one-third showed the usual collapse. Bronchograms were then made and showed no bronchial filling in the upper lobe. Post-mortem intrapleural pressures taken prior to the pneumothorax were much more subatmospheric on the right side than on the left side viz taken at four comparable points the readings on the right side were  $-3$ ,  $-9$ ,  $-7$ ,  $-3$  cm  $H_2O$  and on the left side  $0$ ,  $-1$ ,  $-2$ ,  $0$  cm  $H_2O$ .

*Case 3* The x-ray film showed an airless, contracted right upper lobe. After pneumothorax the lobe showed a selective collapse, was smaller, the homogeneous shadow was denser and the cavities fainter and smaller. Bronchograms were then made and showed normal bronchi and an open cavity. The pre-pneumothorax post-mortem intrapleural pressure was  $-14$  cm  $H_2O$  over the upper lobe and  $-10$  cm  $H_2O$  over the lower lobe.

*Case 4* The x-ray film showed the right lower lobe to be dark and hyperradiolucent and containing a moderate, scattered infiltration. After pneumothorax this lobe showed a 50 per cent collapse and a dense, homogeneous shadow. Bronchograms showed a moderate, saccular bronchiectasis in this lobe. Pre-pneumothorax pressures were  $-1$  cm  $H_2O$  at the base and zero over the apex.

*Case 5* The x-ray film showed a dense exudative infiltration in the right upper lung field with cavitation measuring  $12$  cm. After pneumothorax the upper two-thirds of the lung became a dense, homogeneous shadow through which the rarefactions could be seen faintly. Bronchograms revealed the cavities to be open but most of the bronchi did not fill. Pre-pneumothorax intrapleural pressures at four points on the right side were  $-12$ ,  $-10$ ,  $-12$ , and  $-9$  cm  $H_2O$  and on the left side  $-14$ ,  $-2$ ,  $-3$ , and  $-1$  cm  $H_2O$ .

*Case 6* The x-ray film showed a dense homogeneous left lower lobe with a  $10$  cm cavity. After pneumothorax the dense shadow became even denser but the cavity showed no change in size. Bronchograms showed no filling of the smaller bronchi. Necropsy showed dense, confluent, tuberculous caseous masses a  $10$  cm cavity, small silicotic nodules, considerable fibrosis, tuberculous ulceration of the left lower lobe bronchus and its branches, and no air-containing lung.

Thus, atelectasis occurred in 4 cases of exudative disease, one case of productive disease, and one case of fibroid disease. In 2 cases the bronchi were open and in 4 cases diseased or poorly



filled Emphysema occurred in one case. The intrapleural pressure was greater subatmospherically (more negative) in the five cases taken over the areas subsequently showing the "atelectasis."

### *Alveolar Changes*

The collapsed lung post-mortem showed no roentgen changes differing greatly from that during life (Fig 15). The lung showed collapse to a variable degree and contained air. Bronchograms showed good alveolar filling and necropsy examination revealed air in the alveoli. In some cases, the tracheobronchial tree was first filled with a barium emulsion and then the pneumothorax was begun. During the collapse, air bubbles could be seen moving from the parenchyma through the bronchi to the trachea and larynx.

### *Cavity Changes*

The total number of cavities in this entire group was not counted but reached a considerable figure. However, 25 cavities showed a noteworthy change in size with the pneumothorax.

One cavity measuring 2 x 1 cm was closed roentgenologically. It lay at the level of the seventh dorsal spine and was "closed" by a basal pneumothorax which went as high as the sixth dorsal spine (Figs 9, 10). A large 11 cm cavity just above it was only slightly changed by the pneumothorax. At necropsy the "closed" cavity showed approximation of its walls and the bronchi leading to it were normal and patent.

A gross decrease in size occurred in 24 cavities as measured by their long and short diameters (Figs 4, 5). In this group, 4 cavities showed a decrease in size of from 10 to 25 per cent; they measured originally 6, 7, 11, and 18 cm. Fourteen cavities decreased 25 to 50 per cent in size and originally measured 4, 5, 5, 5, 5, 5, 6, 7, 10, 10, 11, 12, 14, and 16 cm. Six cavities showed a decrease in size of over 50 per cent and originally measured 3, 4, 4, 4, 4, and 9 cm.

Five cavities were distorted in shape by the irregular collapse and the pleural adhesions. One cavity showed no change in size after the collapse but the fluid in it showed a higher level. One cavity could not be seen originally, but was evident after the pneumothorax (Figs 16, 17), two cavities were accentuated (Fig 18), and five cavities were obscured by the pneumothorax.

The factors influencing the decrease in the size of a cavity were noted under the headings of adhesions, infiltrations, bronchial status, and the size of the cavities.

#### (1) Pleural adhesions about the cavity

Large number and dense adhesions—11 cases—average  
approximate decrease in size 25 per cent

Moderate number of adhesions—11 cases—average  
approximate decrease in size 45 per cent

Small number of adhesions—2 cases—average approximate  
decrease in size 70 per cent

Thus the fewer the adhesions the greater was the reduction in  
the size of a cavity

(2) Infiltration about the cavity

Moderate infiltration—6 cases—average reduction 40 per cent

Dense infiltration—18 cases—average reduction 40 per cent

Slight infiltration—no cases

Thus, the density of infiltration was no factor A larger series  
may, of course, have given different results

(3) Status of the bronchi

Five cavities were necropsied Three cases with normal bronchi  
followed down to about a 1 mm diameter showed 40, 35, and 60  
per cent cavitory collapse, two cases having a tuberculous bron-  
chitis showed 15 to 25 per cent collapse

Eighteen cases containing 19 cavities were not necropsied but  
had post-mortem bronchograms Fifteen cavities surrounded by  
normal bronchi showed an average collapse of 35 per cent and

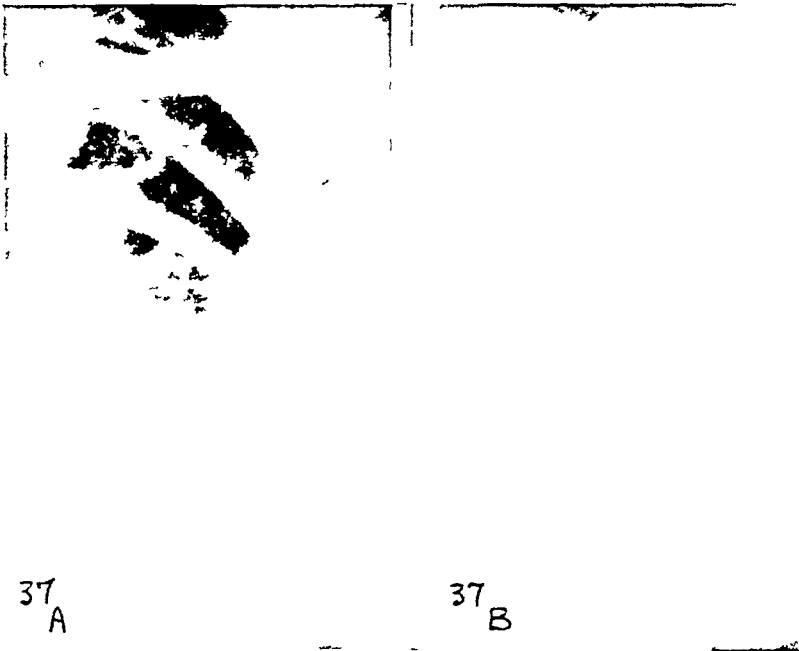


FIGURE 15 CASE 37 Section A shows the postmortem film with a coarse  
nodular lesion at the right base Section B shows a pneumothorax with obscu-  
ration of the lesion and good aeration of the collapsed lung Autopsy confirmed  
the presence of the lesion

three cavities with abnormal bronchi showed an average collapse of 20 per cent

(4) Size of the cavities (long diameter)

Up to 4 cm —6 cavities—average decrease in size 65 per cent

From 4 to 8 cm —9 cavities—average decrease in size 25 per cent

Over 8 cm —9 cavities—average decrease in size 30 per cent

Again—Cavities showing a reduction in size

Up to 25 per cent—4 cavities—Original average size 10 cm

From 25 to 50 per cent—14 cavities—Original average size 8 cm

Over 50 per cent—6 cavities—Original average size 4 cm

Thus, the smaller the cavity the greater was its probable reduction in size

In summary, it appears that the smallest cavity reductions occurred in the presence of many adhesions, diseased bronchi, and large cavity sizes. Conversely, the best reductions were obtained when there were few adhesions, when the bronchi were normal, and when the cavity was small. We feel that we might have "closed" more cavities if we had encountered more cases with less adhesions.

*Changes in Pulmonary Infiltrations*

These changes were noted under the headings of obscuration, accentuation, and concentration of the infiltrations after pneumothorax.

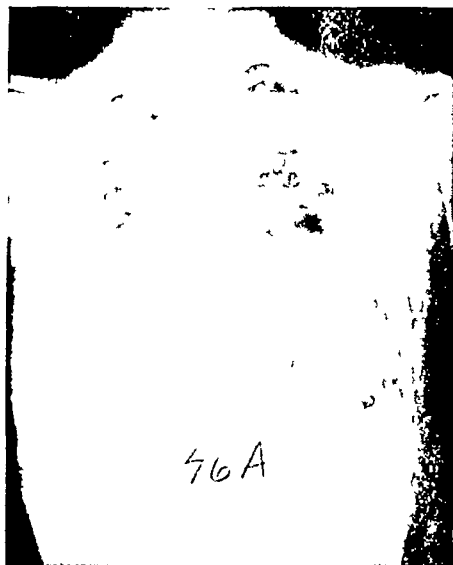


FIGURE 16

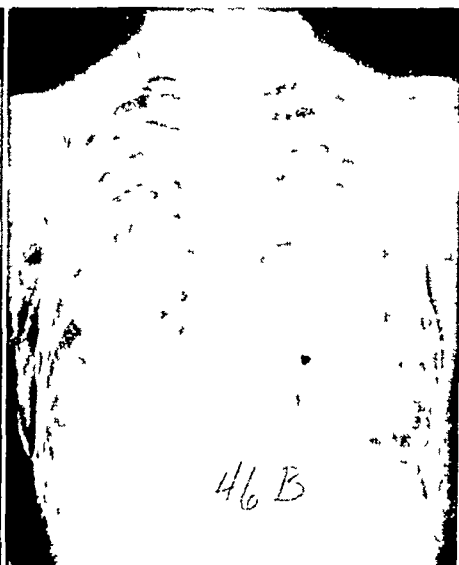


FIGURE 17

Figure 16, Case 46 Postmortem film—Figure 17, Case 46 Bilateral pneumothorax. The right lung shows selective collapse and concentration of the infiltrations. A bronchogram shows good and normal filling of bronchi and alveoli. The left lung shows a cavity with a fluid level not seen previously. Note the shape and position of the heart.

### Obscuration

In 10 cases mild, moderate, and even large infiltrations were much less evident after the pneumothorax (Fig 15) In 4 more cases a light, scattered infiltration could not be seen at all after the collapse The existence of these infiltrations was proved in the 6 cases which came to necropsy

The possible factors were

- (1) In some cases there was actually an increase in the roentgenological surface area of the lung after a partial pneumothorax The diaphragm, in its descent, pulled the base of the lung downward and produced a better apparent aeration of the lung and a greater pulmonary volume
- (2) The pleural air may have had an obscuring effect on some infiltrations
- (3) One case showed a considerable degree of emphysema
- (4) One case showed an increase in the lung area with only a small pneumothorax and little diaphragmatic motion but with a considerable displacement of the heart pulling the lung with it

In all these cases one or more diameters of the lung were increased in size or, one may say, the lung was actually stretched

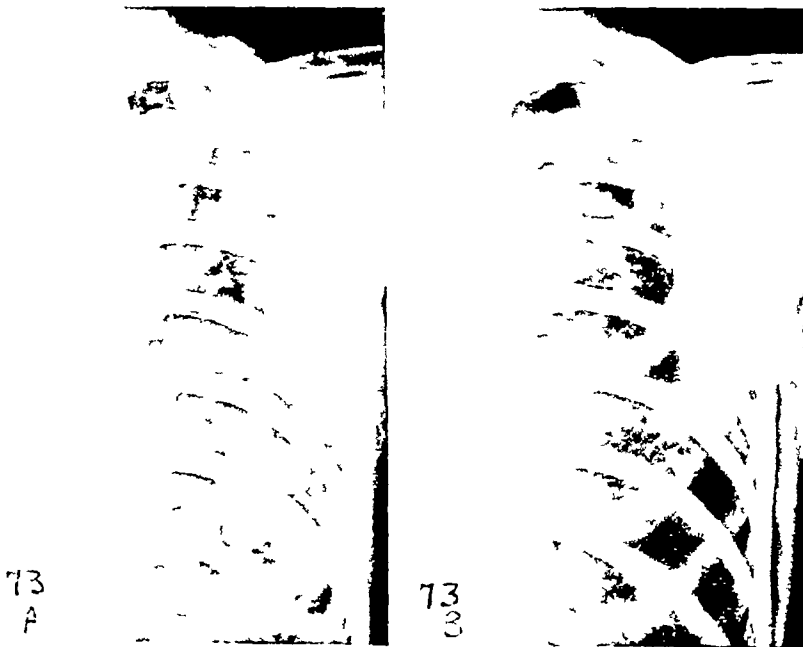


FIGURE 18 CASE 73 Section A shows the postmortem film No cavity could be definitely seen Section B shows a right pneumothorax and a definite cavity

out during the collapse and the apparent increase in aeration may have caused an "emphysema effect" on some of the infiltrations

### *Accentuation*

In 9 cases the infiltrations could be seen more easily after pneumothorax. Both discrete nodular groups and large areas showed this phenomenon.

The possible factors were

- (1) Several cases showed a greater collapse of the more normal lung and the lesser collapsed areas of disease were more prominent.
- (2) In some, the more normal lung became more radiolucent after the collapse due to the stretching of the lung by the diaphragm and the nodules appeared more distinct due to contrast with the surrounding aerated tissue.
- (3) No apparent cause.

### *Concentration*

This was noted in 22 cases (Figs 16, 17). The causes were

- (1) Approximation of the diseased areas by the collapse of the more normal lung tissue between them.
- (2) Selective collapse of diseased areas and fusion of shadows.
- (3) Collapse of the lung generally to occupy a smaller space.

### *Bronchial Changes*

The trachea was often displaced to the opposite side by the pneumothorax. The bronchi were approximated and compressed. In no case was kinking or distortion produced in the larger bronchi. In some cases, when a bronchogram was made prior to the pneumothorax, the very fine bronchi were completely compressed and emptied of the solution, the larger bronchi were narrowed, and the opaque fluid was pushed up into the trachea.

The bronchi were outlined in 155 lungs and in 44 (or 28 per cent) bronchiectasis was present in the bronchi distal to the main cavernous portion of the disease.

### *Effect of the Pneumothorax on the Contralateral Lung*

Of the 39 cases with bilateral pneumothorax, 8 cases showed a decrease of the first pneumothorax when the second pneumothorax was begun. This was due to the shift back of the heart and lung to a more normal position (Figs 7, 8, 12, 13, 14).

Three cases with uncollapsed lungs showed a higher fluid level in their cavities after contralateral pneumothorax (Figs 9, 10). In both cases there was a marked displacement of the heart which may have been the cause.

Three cases with pneumothorax and a marked mediastinal shift showed accentuation of the infiltrations in the non-collapsed lung

### *Pleural Cavity Changes*

In six cases, prior to collapse, the costophrenic angles were clear and no pleural fluid evident. However, after the pneumothorax, fluid was noted and was estimated in the six cases to be from 50 cc to 100 cc (Figs 4, 5). The diaphragmatic pleural reflection showed a normal appearance.

### *Pneumothorax Pressures*

During the pneumothorax the pressure used was high and often reached 100 to 200 cm  $H_2O$ . The end-point of pulmonary collapse was usually indicated by a leak back of air into the subcutaneous tissues. After the pneumothorax was completed the final pleural pressure was not high. In 8 cases with a uniform collapse the final pressure averaged 9 cm  $H_2O$  (0, 4, 6, 8, 9, 10, 12, and 21 cm). In 15 cases with irregular collapse the final pressure averaged 10 cm  $H_2O$  (0, 0, 0, 0, 3, 4, 5, 6, 8, 9, 12, 16, 24, 24 and 34 cm).

### *Aspiration of Pulmonary Cavities*

In over 30 cases a needle was inserted into the cavity through the chest wall and attached to a 30 cc or 50 cc syringe either directly or by an intervening rubber tube. The cavities varied from 4 cm to 12 cm in diameter. Over 20 of these cavities decreased in size when air was sucked out rapidly with the syringe. This decrease in size amounted to 50 per cent or more and lasted from 5 to 60 seconds, after which the cavity returned to its original size. The cavity wall, in many cases, became perceptibly thinned during this decrease in size and the surrounding tissues filling the space became highly translucent.

The factors involved in the phenomenon were

- (1) *Size of the draining bronchus* In most of these cavities the bronchus was outlined by an intracavitary injection of a barium mixture which would always overflow into the bronchial tree. This would show the size of the bronchus and also the air bubbling from the trachea into the bronchus and then into the cavity shortly after suction was made. The smaller the bronchus the longer was the period of time the cavity remained small. In a number of cases the bronchus was partially obstructed with a very thick barium mixture and, in these cases, the cavity would remain small in size up to five minutes—until enough air was sucked into the cavity through the bronchus to allow it to regain its original size.

- (2) *The rapidity and degree of suction* The more rapidly the air was sucked out the smaller the cavity became—again, until enough air came in via the bronchus
- (3) *State of the nearby tissues* By this term we include both the cavity wall and the surrounding lung That the cavity wall was not all caseous tissue, but in many cases was composed chiefly of collapsed alveoli, was shown by the thinning of the cavity wall during the decrease in the size of the cavity This occurred in even very large cavities The degree of decrease in size was influenced also by the amount of normal lung tissue about the cavity Normal tissue was necessary to fill up the space left void by the shrinking of the cavity

Thus, the narrower the bronchus, the greater the suction, and the more normal adjacent lung tissue present, the greater was the decrease in the size of the cavity subjected to aspiration

### *Discussion*

Just as in pneumothorax in the living, the post-mortem effects on the *bony thorax* included an elevation of ribs, sternum and clavicle, a widening of the intercostal spaces, and an increase in the frontal and lateral diameters of the thorax In the living, the process is due to neuromuscular action In the dead thorax, the mere increase of intrapleural pressure caused the upward motion of the ribs since that is the only direction in which they could move The same phenomenon is seen in dead animals whose lungs are inflated and deflated through an endotracheal cannula, during inflation the ribs are elevated and the other effects follow Thus, the inspiratory movements of the chest cage may be produced not only by neuromuscular elevation of the ribs but also by the mechanical increase in the intrapleural pressure and by inflating the lungs

The descent of one leaf of the *diaphragm* during post-mortem pneumothorax affected the other leaf to only a very slight extent The same picture is seen in pneumothorax in the living and after paralysis of a leaf After a phrenic nerve interruption, the paralyzed hemidiaphragm has its action determined by pleural and peritoneal pressures and is not directly affected by the other leaf Since the post-mortem effects are mechanical in nature, it stresses the fact that the diaphragm may be regarded functionally as two separate muscles, each leaf having not only an independent nerve supply coordinated in the central nervous system but also an independent mechanical action due to its peculiar anatomical structure

The *heart* showed a surprising degree of mobility and pliability

in this study A pneumothorax displaced the heart to the other side and a contralateral pneumothorax replaced it in its original position Descent of one leaf of the diaphragm caused little or no descent of the heart, but a descent of both leaves pulled the heart downward and changed its shape The picture so produced resembled that seen in emphysema, a small "drop" heart even when it was actually enlarged, and again stresses the purely physical aspects involved

Pleural *herniation* through the anterior and posterior mediastinums behaved post-mortem similarly to that seen in living cases It occurred frequently and was reduced by a contralateral pneumothorax Both anterior and posterior mediastinal "weak spots" were crossed by the pleural membranes under increased intrapleural pressure and this mechanical action is probably sufficient to explain its occurrence in the living patient

As expected, the type of *collapse* showed great variations due largely to the number and extent of pleuro-pulmonary adhesions and, in relatively free pleural spaces, surprisingly good collapses were obtained In the living person, pneumothorax causes a diminution in the lung volume due to its elasticity and tendency to retract to its solid airless capacity And in this study, the dead lung was sufficiently elastic and was reduced to a smaller volume by the positive pressure pneumothorax forcing out much of the air from the alveoli In both the living and dead lungs there was a reduction of alveolar air in the living, by the retraction of the lung caused by the increase in intrapleural pressure even though at a subatmospheric level, in the dead, by a slight initial subatmospheric retractility followed by hyper-atmospheric pressure forcing out the alveolar air Thus, the mechanism of pulmonary collapse has similar features in both living and dead

The *factors* determining the degree of pulmonary collapse included the pleural adhesions mentioned above and several intrapulmonary ones Thus, in a relatively free pleural space, the degree of pulmonary infiltration and the size of the pulmonary caverns had a direct bearing on the collapse Lungs with a mild infiltration showed an average collapse of 60 per cent whereas those with extensive disease showed a 45 per cent collapse Cases with no pulmonary cavities showed an average collapse of 60 per cent and those with cavities showed a lesser collapse depending directly on their size Conversely, the greater the amount of normal tissue present the greater was the collapse obtained The inherent elasticity and retractility of the lung was undoubtedly a factor but could not be measured The time that the pneumothorax was done, which ranged up to three hours after death, was not a factor in this group of cases



*Selective pneumothorax collapse* occurred in 14 lungs and presented a picture similar to that seen in the living. Two lungs showed a pre-existing lobar atelectasis. In the four cases autopsied the bronchi to the selectively collapsed lobes were grossly normal and patent. Extensive disease was present in 12 of the lobes selectively collapsed, miliary disease in one, and a light infiltration in one. The selectivity of the collapse occurred with even small amounts of air and was strikingly demonstrated fluoroscopically. One infers that either (1) it was easier to force the air out of the involved lobe, or (2) the tissues in that lobe were under greater elastic tension and so retracted first and most. In the 12 cases with extensive disease the remaining normal tissue in the lobe and the few remaining elastic fibers must certainly have been under greater than ordinary tension and so collapsed first and most when released by the pneumothorax. Why the two cases with miliary disease and the light infiltration showed the same phenomenon cannot be explained. It is our impression that the selective collapse seen in this study was due to the increased elastic tension of the normal tissue about the diseased areas and was present prior to the collapse.

There are several theories regarding the mechanism of selective collapse in the living patient and some stress the absorption of alveolar air and the respiratory motion of the lung. Of course, selective collapse as seen in this group of dead lungs may not be identical with that seen in the living for, in this series, selective collapse occurred almost instantly whereas in the living it may be immediate or it may be delayed for several weeks. The purely mechanical explanation of the normal tissue under greater stretch would apply to the group showing immediate selective collapse. It is more difficult to explain the delayed group unless one supposes that elastic tissue changes take place later in the involved lobe due to increasing fibrosis, slowing of the lymph flow, and anoxia of the tissues. At any rate, it stresses the mechanical factor involved in selective collapse as certainly the dominant one if not the complete cause in itself.

The term *atelectasis*, as used here, denotes that a lobe is decreased in size, appears "roentgenologically airless," and is seen as a dense homogeneous shadow. This occurred in 6 cases in this study and, in 2 of them, it existed prior to the pneumothorax. Whether all these cases showed a true complete airlessness anatomically is not known but the one case necropsied did show it. The other 5 cases presented the characteristic roentgen features seen in typical examples in the living. Some cases of lobular atelectasis may well have occurred also but were excluded to avoid confusion. The chief features present were (1) extensive disease

in the lobe involved, (2) the bronchi could not be filled by bronchography in 4 cases, showed ectasis in one case, and were normal and patent in one case, and (3) the intrapleural pressure over the involved lobe was greater subatmospherically in the 5 cases in which measurements were made

In the living patient, atelectasis is caused by either bronchial obstruction or by occlusion of the arterial blood supply. However, some cases seen in chronic pulmonary disease show no obvious bronchial block or vascular interference and may be due to an old transient bronchial block, or to a collapse of the alveoli resulting from a blocking of numerous microscopic bronchioles, or perhaps other obscure causes. In the cadaver bronchial block should prevent the escape of alveolar air and certainly no air could be absorbed by the blood. One must suppose then that, in these cases, the atelectasis must have existed prior to the pneumothorax and was only accentuated by it. Any air present in the lobe occurred in cavities and in more normal segmental sections. The existence of a higher subatmospheric pressure over the lobes involved shows that they were already under great elastic tension. The pneumothorax released this tension and the atelectasis became more pronounced.

The normal *parenchyma* of the lung showed a similar roentgen appearance under post-mortem pneumothorax to that seen in living cases. Some cases showed a better aeration of the non-collapsed areas after the pneumothorax than previously, due apparently to the stretching of the lung by the diaphragm and its increase in an apex-base direction. The alveolar air was in direct communication with the atmosphere as shown by the ease of filling the alveoli with radiopaque solutions.

*Cavity changes* were common. Only one small cavity was "closed" in this series and 24 were made appreciably smaller. The greater the size of the cavities and the more extensive the pleural adhesions the less was the decrease in size under collapse. The presence of diseased bronchi also limited the decrease in the size of the caverns. The degree of infiltration about the cavities proved to be no factor but we feel that a larger series may have given different results. The rigidity of the cavity walls was undoubtedly an important factor but was not evaluated. Under more favorable conditions more cavities might have been "closed." It stresses the mechanical factors in the reduction of the size of the cavity post-mortem. Its application to the living pathology may be considerable. In the living patient, cavity closure is often a complex process and this study stresses the common concept that, at least, the initial reduction in size with pneumothorax (or even other

collapse measures) is due to the mechanical release of the tension of the tissues about and forming the cavity wall

As often seen in the living patient, some cavities showed distortion by pleural adhesions, elevation of their fluid levels, or were made more evident, or were obscured. The practical applications of these phenomena in interpreting disease processes by roentgen films in the living patient is evident.

Changes in the *pulmonary infiltrations* under pneumothorax occurred commonly. The *disappearance* of some infiltrations after pneumothorax was due probably to an "emphysema" effect caused by an actually better aeration of portions of the lung and the presence of air in the pleural cavity. The actual existence of these infiltrations was proved at necropsy. The clinical application is obvious in that such an event might be regarded as the rapid healing of a lesion under collapse. The *accentuation* and *concentration* of other lesions was discussed in the text.

The pneumothorax caused a displacement of the trachea similar to that of the heart. The larger *bronchi* were narrowed and approximated, as seen by the instillation of radiopaque solutions. The very small bronchi were often completely shut out by the approximation of their walls. No kinking or distortion occurred in larger and medium-sized bronchi. The main site of the parenchymal disease showed some bronchial abnormalities in almost all cases and the distal and less-diseased areas (usually lower lobes) showed bronchiectasis in 28 per cent of the lungs.

The effects of the pneumothorax upon the *contralateral lung* were slight and negligible in most cases but several cases showed appreciable changes such as accentuation of infiltrations and a higher fluid level in cavities. The marked displacement of the heart in these pneumothoraces may well have been the cause.

The *aspiration of cavities* post-mortem is of interest. A large number of the cavities were reduced in size for short periods of time. The factors involved were discussed in the text. The several important observations in this experiment include (1) the number of even very large cavities that were reduced in size, (2) the greater the bronchial occlusion the smaller the cavity became, (3) many supposedly thick, rigid, caseous cavity walls became markedly thinned and then returned to the original state, and (4) the surrounding normal alveolar tissue enlarged to fill up the space left by the decreasing cavity.

The thinning of the thick caseous walls demonstrated the surprisingly large amount of atelectatic alveoli forming the wall—much more than was suspected even at necropsy in both gross and histologic studies. This factor may have an important bearing in the living—in the production and healing of cavities, in the

rapid changes in the size of cavities, in the changes in thickness of cavity walls, in changes in the intrinsic pressure mechanics in the lung caused by the collapse and aeration of such areas, and in the effects such changes may have upon the physiology of the cavity wall and its vascular relationships. The ability of the surrounding normal tissue to enlarge and present a picture of "localized compensatory emphysema" may add to the probabilities mentioned.

### SUMMARY

1) Artificial pneumothorax was produced in cadavers and many of the results were identical with those seen in pneumothorax in living patients.

2) The chief effects so produced included mobility of the chest cage, descent of the diaphragm, mobility of the heart, transmediastinal herniation, selective collapse, atelectasis, reduction in the size of pulmonary cavities, and changes in parenchymal infiltrations.

3) These findings contribute to the physics of pneumothorax and stress the importance of the purely mechanical factors involved.

4) The clinical application of these observations are of particular value in the roentgen interpretation of disease processes and changes.

### RESUMEN

1) Se produjo neumotórax artificial en cadáveres y muchos de los resultados fueron idénticos con los que se obtienen en el neumotórax en pacientes vivos.

2) Los principales efectos así producidos incluyeron movilidad de la caja torácica, descenso del diafragma, movilidad del corazón, hernia transmediastínica, colapso selectivo, atelectasia, reducción en el tamaño de cavernas pulmonares y alteraciones en infiltraciones del parénquima.

3) Estos hallazgos contribuyen a nuestros conocimientos físicos del neumotórax y recalcan la importancia de los factores puramente mecánicos que los producen.

4) La aplicación clínica de estas observaciones es especialmente valiosa en la interpretación de procesos y alteraciones morbosas en la radiografía.

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# The Pathogenesis of Primary Atypical Pneumonia

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The term atypical pneumonia, etiology unknown, includes the following Atypical pneumonia with leukopenia, atypical broncho-pneumonia of unknown etiology, acute interstitial pneumonia, virus pneumonia, acute pneumonitis, pneumonitis, disseminated focal pneumonia, and acute influenzal pneumonia

The disease has come to be written about only within the past decade It gained widespread recognition in World War II Because of its nature and close similarity to other respiratory diseases, just where and when it first existed is at present unknown It has been stated that it is probably not a new disease, inasmuch as a description of a closely similar malady dates back seventy-five years

The etiology of atypical pneumonia is obscure It is thought by many that a filtrable virus is the etiological agent but this hypothesis has not been proved Others believe that two agents, one presumably a virus and the other a bacterium may possibly act in concert to produce an infection different from that which would be produced by either alone Still others feel that several etiological agents are involved and that therefore primary atypical pneumonia is a syndrome rather than a true entity Most cases reported are in the young adult population, both male and female The great majority of cases are in young males in the second and third decades of life

The cyanosis and dyspnea sometimes noted when the pulmonary process is extensive and bilateral appears to be due to *anoxemia* rather than *toxemia* such as seen in cases of lobar pneumonia Some patients do not appear ill at all Often we are surprised at the paucity of clinical and physical findings when correlated with x-ray evidence of considerable consolidation and early there is apt to be a normal pulse and respiration

The fundamental pulmonic lesion is an acute interstitial pneumonitis The pathological change in the involved portion of the lung is essentially a serofibrinous exudation with secondary inflammatory hyperplasia Only an inteistitial involvement in the lung would produce such a combination of roentgen and physical

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findings First, the alveoli would be air bearing early in the course, giving essentially normal pulmonary resonance and no rales, but the interstitial fluid would add to the density of the lung as seen in the roentgenogram Second, by swelling, and stasis, eventual seepage into the alveoli producing the moist rales and the "wet lung" picture could occur Third, the interstitial swelling with stasis and the wetness of the alveoli would account almost quantitatively for the anoxemia, cyanosis, and dyspnea whenever they occur Fourth, that diapedesis does not occur with subsequent consolidation within the alveoli is attested by the presence of muco-tenacious sputum only occasionally tinged with bright red blood instead of the typical rusty sputum seen in pneumococcus pneumonia Fifth, the absence of toxic action on the pulmonary capillaries' bed and the low systemic toxicity are in the same direction Sixth, this series of events is consistent with the roentgen findings, throughout the course of the disease Seventh, in these described pneumonitic areas, mixed bacterial flora from the upper respiratory tract find a tissue of lowered resistance and an excellent culture media for secondary invasion The pathological process may then center about the bronchioles, which become filled with pus and desquamated cells from the lining, which is partially or completely destroyed Classical physical findings of consolidation are not found

There is no definite characteristic roentgen appearance of this disease of the lung The density is hazy, soft and extends outward from the hilus well into the parenchyma, occasionally reaching the periphery The appearance is that of a confluent mottled or rounded area, usually of homogenous moderate density in the central portion, with the borders fading into the normal lung It is similar in roentgen appearance to the exudative inflammation around a lung abscess The density is not as marked as that seen in cases of lobar pneumonia, nor is the periphery of the lesion as well defined The opaque areas suggest air bearing lung

Cold agglutination tests are positive in a great majority of individuals suffering from primary atypical pneumonia The technique of testing for cold agglutinins varies a great deal with different technicians but in general the test becomes positive in a "diagnostic" dilution between the third and seventh day of the illness The maximum titer of the agglutinin is reached in two weeks following which a decline in strength is noted

Therapy, other than that of a supportive nature, has proved discouraging Convalescence is often delayed Slow resolution of the pneumonitic areas and migration to previously unaffected areas are common Treatment which would prevent either, would materially reduce the man hours lost through this disease

From a consideration of the above fact, it is postulated that the changes in atypical pneumonia can be explained on a mechanical basis rather than on an infectious one, although secondary bacterial contaminations and complications in the involved lung can and do occur

In 1943, while having the dual experience of being in charge of a blood bank, as well as the observation of patients on a pneumonia ward, I was impressed with the cold agglutination which sometimes interfered with our crossmatching of atypical pneumonia patients needing blood transfusions. These reactions often occurred at room temperatures. On the ward I was also impressed by the fact that dyspneic patients suffering from atypical pneumonia often did poorly in oxygen tents in which the temperature was quite low. The pneumonia, often, under these circumstances spread rapidly and migrated to uninvolved portions of the lung and to the opposite lung. In a study of fatal cases of the disease in the literature one is further impressed by the fact that these patients were placed in oxygen tents where the pneumonitic process increased until death resulted.

It is therefore postulated that the immediate precipitating factor in atypical pneumonia is autohemoagglutination in the patient's own lung capillaries.

Cold agglutinins have been found to have a wide thermal range of reactivity. Of the large internal organs, the lungs hold the unique position of being in intimate contact with the atmospheric air through the respiratory passages. The pulmonary capillaries form the richest capillary network of the body, the meshes of which are smaller than the vessels themselves. These plexuses lie immediately in the walls of the alveoli either directly exposed to the air or lying under the thin lining epithelium of the alveoli. The network of capillaries form a single layer which is usually common to two or more adjacent alveoli. During quiet respiration, the tidal air amounts to about 500 cc, which is about  $\frac{1}{8}$ th of the total amount that can be respired. This fresh atmospheric air reaches the alveoli by diffusion which allows adequate time for the air to be warmed to body temperature. The minute vessels of the lung are thus unlike those of any other vascular area, surrounded by and practically in contact with air. As severity of exercise increases, hyperpnea results and merges into dyspnea. In healthy individuals the total amount of air drawn into the lungs with each inspiration may be equal to the tidal, complementary, and supplementary air or 4,000 cc. This dilutes a residual air of perhaps 1,000 cc. The total minute volume of air may be as much as 160,000 cc. After such deep inspirations, the respiratory bronchioles and alveolar ducts receive fresh atmospheric air. The

advancing margin of the latter however, as a result of its spike form, is prevented from coming in direct contact with the respiratory epithelium by a layer of vitiated (alveolar air). However because rapid diffusion and mechanical mixing the temperature of the air in contact with the pulmonary capillaries must be lower than body temperature. As a corollary of this, the lower the outside atmospheric temperature the lower must be the temperature in contact with the respiratory epithelium at a given minute volume of respired air, if this minute volume is greater than that in a resting state.

The fallacy of assuming that *in vitro* test results with cold agglutinins are comparable to *vivo* findings, is at once apparent. Agglutination in a 1 to 8 dilution of blood plasma is considered significant. However, such dilution does not occur *in vivo*. Another point which is not often considered is that *in vitro* tests for cold agglutination the red blood cells are often 1 to 40 or 50 the number they are in the body itself. Capillaries are very small,  $\frac{1}{2}$  to 1 mm in length and up to 10 microns in diameter. A capillary may be so contracted that a red blood cell is unable to enter without undergoing deformation. A red blood cell pressed into an elongated or sausage-like form can frequently be seen within a capillary or even imprisoned by the complete closure of the capillary lumen at each end. In other instances constrictions of the vessel excludes the corpuscles entirely from a neighboring capillary channel, the plasma alone being permitted to pass. This phenomenon is called "plasma stripping" and concentrates increased proportions of red blood cells in other areas. The ready distensibility of the vascular bed of the lungs accounts for the fact that little or no rise in pulmonary arterial pressure occurs during muscular exercise, despite the great increase in cardiac output. It is believed that a fair value for pulmonary capillary blood pressure is 10 mm of mercury and that this pressure in the lung capillaries is extremely hard to disturb because of the immense area of the vascular net and the readiness with which expansion can be induced. Since the red blood cells barely make their way through the capillaries any increased agglutinative tendency or stickiness caused by contact with air cooled below body temperature may cause them to block a capillary channel.

This process would be different from atelectasis in that it is not a collapse and early the alveoli are open. Such a process would begin a vicious cycle and tend to procreate itself.

Thus we see that in dyspnea the pulmonary capillary blood pressure already low, is not raised and the blood continues its slow course through the lungs. The air in contact with these capillaries may be lower than body temperature and the degree



is related to the temperature of the outside atmospheric air and the minute volume of respired air. A cold agglutinin of the red cells is activated by this lowered temperature and agglutinates in the capillary, the process becomes wide spread and we have primary atypical pneumonia. The process extends outward from the hilum since, as the air passes toward the periphery of the lung, it becomes increasingly warm. It affects young males mainly since they are more apt to have vigorous exercise out of doors than other groups.

Hemorrhagic areas (hemorrhagic encephalitides), have been noted in the brain and other areas in fatal cases of atypical pneumonia. These could theoretically be caused by clumps of red blood cells washed from the lung capillaries and lodging in the various localities.

Perhaps we will find that cold agglutinins are much like the Rh factor. A certain proportion of individuals may have cold agglutinins and agglutinogens, not detected by present day laboratory methods, and these become activated under certain conditions to produce pathological changes in the lung, or perhaps certain bacteria and viruses cause cold agglutinins to appear and indirectly are responsible for the pathological changes. The marked activity of the autohemagglutinins is dependent on an increase in the concentration of some normal serum constituents. This may occur in response to infections with a variety of agents and may be related to the tissues involved.

If this hypothesis is true, and it can fairly easily be proved or disproved, it is an important contribution to the field of medical science. Treatment of those individuals with atypical pneumonia by their breathing air warmed to body temperature would prevent migration of the pneumonia to other uninvolved areas, and slow resolution of involved areas. Prophylactic treatment could prevent many cases from developing.

### SUMMARY

1) A new concept is presented to explain the pathogenesis of primary atypical pneumonia.

2) Supportive evidence for this theory is introduced from various branches of medical science.

3) It is believed that this presented concept can be fairly easily proved or disproved where cases of atypical pneumonia are available for study.

4) If this concept of the development of atypical pneumonia is correct, it will be an important contribution to present day medical science.

5) Methods of treatment and prophylaxis of atypical pneumonia

will proceed on firm ground once a knowledge of the pathogenesis of the disease is obtained.

### RESUMEN

1) Se presenta un nuevo concepto para explicar la patogenia de la neumonia atípica primaria

2) Se aducen pruebas obtenidas de varias ramas de la ciencia médica que sostienen esta teoría

3) Se opina que el concepto presentado puede ser fácilmente comprobado o confutado cuando existen casos de neumonía atípica que pueden ser estudiados

4) Si este concepto del desarrollo de la neumonía atípica es correcto será una contribución importante a la ciencia médica actual

5) El tratamiento y la profilaxia de la neumonia atípica reposarán sobre una base firme cuando se obtengan conocimientos de la patogenia de la enfermedad

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# The Significance of Pleural Effusions as Indicating the Presence of Abdominal Disease\*

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About five years ago we were impressed by the frequency with which we were seeing individuals with abdominal distress in whom we found inflammatory, malignant, or nonmalignant lesions of the organs of the abdominal cavity, with or without ascites, and associated with the following physical signs at either base of the lungs

- 1) Decreased tactile fremitus,
- 2) Impaired resonance to flatness, not altered by deep inspiration,
- 3) Increased resistance to the percussing finger in these areas,
- 4) Seldom was there any marked change in the breath sounds, except at times there was a slight diminution in their intensity,
- 5) There was no alteration in voice transmission, egophony was not present

In the early cases that we saw we thought that these were produced by atelectasis due to the accumulation of intra-abdominal fluid elevating the diaphragm. But later on found them in infectious or malignant lesions of the abdominal cavity in which only small amounts or no fluid was present in the abdomen

For many years, on the medical service at the Buffalo General Hospital, Doctor Nelson G Russell Sr was doing many chest taps with vacuum tubes without any untoward results, and finding a high percentage of fluids in the pleural cavity in various conditions. It was his skill in interpreting these physical signs that led us to make these taps with so many positive results. This was being done well before the x-ray became so valuable in revealing the presence of fluid, and was based on the physical signs we have mentioned. It is generally recognized that fluid at the base and early atelectasis are difficult to distinguish from each other, and here the exploratory tap was of greatest value

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Most textbooks state that it takes between 300 to 400 cc of fluid to be present in the thoracic cavity to be recognized, and about 600 cc in the abdominal cavity. We feel rather certain that we have been able to find smaller amounts of fluid present in both cavities, and proving their presence by abdominal or thoracic aspiration. With this background and the group of patients we have mentioned increasing in number, we performed more taps with positive results, and should like to present our methods of examination of the abdomen and chest, technique of collecting the fluid, the character of the fluids withdrawn, and their diagnostic significance.

### *Physical Examination*

In all patients the well-known signs of fluid were sought for, and in many they were present. We found, though, that the following methods were valuable, and we believe have elicited one which may not have hitherto been emphasized. In our experience, it has been easier to demonstrate the presence of a medium amount of fluid in the abdominal cavity by having the patient stand for the performance of the fluid transmission wave. We believe that in the erect position the pelvic cavity is filled above the brim by a quantity of fluid which when the patient is supine fills the abdominal cavity without coming up far enough laterally to produce adequate fluid transmission or shifting dullness. Attention was called to this by Robert L. Pitfield, of Philadelphia, some years ago.

A physical sign that we have elicited in a number of these cases, where a large amount of fluid was present in the abdomen and a smaller or large amount was present in the left chest cavity, is demonstrated as follows. Placing the left hand on the anterior abdominal wall well down towards the pubic region and with direct percussion over the left thoracic cavity posteriorly from the scapula down with the right fingers, when one reaches the level of the fluid in the chest cavity, the percussion impulse is transmitted through the fluid in the chest, through the diaphragm, through the abdominal fluid to the left palpating hand on the anterior abdominal wall. In other words, there is a continuous column of fluid which is an excellent transmitter of percussion waves. This has been of value in demonstrating fluid in both the abdominal and thoracic cavities. We have not elicited this sign as readily when the right chest cavity is involved, due, we believe, to the interposition of the liver.

### *Method of Securing Fluids*

All of our fluids from the chest and abdomen have been secured by using the vacuum tube or a 20 cc syringe with a 16

to 18 guage 1½ to 2 inch needle, straight or short bevel We have withdrawn the peritoneal fluids with the patient in either the standing or sitting position We have used ethyl chloride spray only for anesthesia purposes in securing fluids In 104 pleural and 100 peritoneal aspirations we have had no accident due to injury to the lung, pleura or abdominal contents

We have performed this abdominal tap just before surgery, and have investigated the peritoneal surfaces and the abdominal organs in the vicinity of the tap, and found no evidences of hemorrhage or trauma Under these circumstances, we believe that it is not necessary to use a trochar to secure fluids for diagnostic purposes from the abdominal cavity Even when fluid is not present in the abdominal cavity the insertion of a needle of this size and type has not been associated with trauma In a personal communication from Dr J A Bergen, he stated that following the injection of various vaccines to stimulate the peritoneal response in patients with ulcerative colitis they had not injured the intestinal canal

In aspirating fluid from the left chest, and in the presence of ascites, one must be sure that the needle is inserted high enough



FIGURE 1

to be well above the level of fluid in the abdominal cavity so as to be certain we are not withdrawing fluid from the abdomen In none of our cases did we find empyema present

### SELECTED CASE REPORTS

#### *Inflammatory Lesions in the Abdomen Associated with Fluid in the Pleural Cavity and Combined Symptomatology*

The presence of fluid in either pleural cavities is associated with fever, leucocytosis and an increased sedimentation rate when the etiological factor in the abdominal cavity is inflammatory in type We should like to present the following case of this type to demonstrate these findings

*Case 1* A physician, 52 years old, had considerable distress and discomfort of five week's duration, in the left upper abdomen and pain in the left side at the costal margin, urinary frequency, pain in the left lower chest posteriorly not associated with respiration

Physical examination revealed a temperature of 100°, pulse 83, respirations 22 There was tenderness over the left kidney, impaired resonance at the left base not altered by deep respiration, and a small amount of clear fluid was removed, which on culture and sedimentation studies was negative White blood count, 12,100, 77 filaments, blood culture, negative, negative urine, negative urogram with skiodan

X-ray examination of the chest suggestion of an elevation of the left hemidiaphragm A flat film of the abdomen revealed some bowing of the spine to the right and a disturbance in the psoas muscle shadow The diagnosis was made of a perinephritic abscess close to the left diaphragm with fluid formation in the left pleural cavity due to inflammatory reaction beneath the diaphragm Surgical drainage of the kidney area was done and a perinephritic abscess was found

This was one of our first cases in which we correlated early the accumulation of fluid in the pleural cavity secondary to an inflammatory lesion beneath the diaphragm Since this time, we have accumulated 6 cases of fluid in the right pleural cavity due to a subdiaphragmatic abscess secondary to a perforated peptic ulcer, post-cholecystectomy, ruptured appendix, and one due to amebiasis

#### *Right-Sided Pleural Effusion Secondary to a Right-Sided Subdiaphragmatic Abscess*

*Case 2* A young man of 34, had rheumatic heart disease with aortic insufficiency and duodenal ulcer Two days previous to his admission to the hospital, he was seized with severe epigastric pain, nausea and emesis, with chills and fever and burning on urination There was no darrohea He had not worked for one year previous and had never been outside the city of Buffalo

Physical examination by several examiners revealed tenderness in the mid-epigastrium, more marked over the liver, which was enlarged He was slightly icteric There was impaired resonance at the right base An enlarged liver and spleen developed The right hemidiaphragm showed

fixation, and there appeared to be a small amount of fluid in the right hemithorax

The leucocyte count went to 38,000, 60 bands, 36 filaments, icteric index, 20, sedimentation rate, 50, Urinalysis was negative. A pleural tap showed the presence of a clear yellow fluid in the right hemithorax

Hepatitis was considered as a possible diagnosis. With the appearance of fluid in the chest, which was removed, cultured and imbedded and found to be negative, a diagnosis of an inflammatory lesion beneath the right diaphragm with inflammatory response in the pleural cavity was made. Etiological source being undetermined, a ruptured peptic ulcer was suspected. Drainage of the abscess was instituted by the surgeon, a fistulous tract developed, and while under the observation of the surgeon, its persistence made him suspect that it might be due to amebiasis. He made the necessary studies and demonstrated the presence of motile amoeba in the drainage fluid, and a complete response was made to the administration of emetin.

### *Right-Sided Fluid Due to Perforated Peptic Ulcer*

*Case 3* A male, 56 years old, with a previous history of a peptic ulcer 25 years ago, and a resection of his caecum for a carcinoma 5 months previously entered the hospital complaining of severe epigastric distress which occurred very suddenly. The abdominal pain was described as being rather steady than sharp, it lasted for 1½ hours when he received a hypodermic injection of morphine. Vomiting of fluid and solid particles, and several loose stools were noted.

The immediate physical examination revealed a small amount of tenderness in the region of the scar of his resection. No diagnosis was made at this time, except consideration was given to acute gastroenteritis, perforated abdominal viscus was considered unlikely. Four days later diffuse epigastric abdominal tenderness was observed, and six days later it was noted that he had considerable hiccoughing. There was limitation of motion of the right hemidiaphragm. Pleural friction sound was heard, and the diagnosis of diaphragmatic pleurisy was suggested. Flat films revealed no free air in the abdominal cavity. Physical examination at that time revealed impaired resonance at the right base with the possibility of fluid considered. Tap performed, and slightly cloudy yellow fluid was withdrawn. X-ray demonstrated partial obliteration of the costo-phrenic angle, some pleural thickening, some streaky atelectasis.

Fifteen days after admission a large subphrenic abscess was drained and subsequently, fluid was found at the right costo-phrenic sinus. The patient returned home in four weeks.

In 8 weeks he was re-admitted to the hospital, and he had definite evidence of dullness and a few rales at the right base. X-ray film showed an obliterative pleuritis as well as a definite fluid level between the liver and the diaphragm. Through the old incision, another small localized abscess was drained.

These three cases are examples of patients originally presenting symptoms of upper abdominal distress and discomfort associated with localized signs in the abdomen and chest, and representing an inflammatory reaction on the pleural surface of the diaphragm.

and the pleura covering the lung and an accumulation of fluid in the pleural space Ochsner called attention in 1,380 cases of subdiaphragmatic abscess, pleurisy with effusion occurred in 388 on the affected side

### *Abdominal Fluid Associated with Benign Pelvic Tumors*

Woman, 71 years old, with increasing swelling of the abdomen in the past 5 years Patient noticed a year previously, a sense of pressure and fullness in the lower anterior chest with marked exertional dyspnoea Had gained 18 lbs in the past three years, no cough The abdomen showed definite distension with fluid, liver and spleen not palpable, fluid wave readily demonstrable with shifting dullness Diagnostic abdominal paracentesis was done, and 50 cc of clear yellow serum was secured Examination of the fluid was negative for micro-organisms and malignant cells Examination of the chest revealed impaired resonance of the left base, some distant coarse rales at both bases, a small amount of fluid was present in the left chest cavity A firm irregular mass was present in the pelvis An x-ray film of the chest was negative The differential diagnosis lay between a malignant tumor of the pelvis with implants on the peritoneal surfaces and pulmonary metastases, or a benign tumor associated with ascites and hydrothorax On opening the abdomen, 700 cc of clear serous fluid escaped, and benign bilateral ovarian cystomas were removed

In 1937 Meigs called attention to a group of cases in which ascites and hydrothorax was associated with fibroma of the ovary In July 1943, in a subsequent article, he called attention to the fact that in 1937 Muriel B McIlrath located a report by Lawson Tait, who in 1892 described a patient with left-sided hydrothorax and ascites associated with a large solid growth of the right ovary The removal of this tumor resulted in a complete recovery Tait states, "The striking result obtained in this case has gone a long way to confirm me in the advisability of extending the principles of exploratory incisions in the abdominal disease to an almost universal application"

Since Meigs called attention to this syndrome, a number of these cases have been reported, and the emphasis has been placed upon the fact that the presence of a pelvic tumor and ascites and hydrothorax does not necessarily mean carcinoma in the abdomen with pulmonary metastases Meigs stated that benign tumors of the ovary should be considered an etiological factor, and may cause a simultaneous collection of fluid in the abdominal and chest cavities

Our patient represents a combined symptom complex of abdominal distress and thoracic distress with no evidence of vascular or pulmonary disease to account for it, with a small amount of effusion in the left chest and ascites, secondary to a benign tumor of the ovary



In the complete discussion of the presence of fluid in the abdomen with dyspnoea, abdominal pain, and abdominal tumor, Meigs and others state that it is not known why fluid accumulates in the abdomen and pleural spaces. There is no inflammatory reaction in the abdomen or chest in these patients. Serum protein determinations in his cases and our own have been found normal to rule this out as an etiological factor, and there have been no cardiac or renal conditions present.

Pinner and Moerke, in a careful review of the etiology of pleural effusions, came to the conclusion that the pleura is highly permeable in either direction for the constituents of the blood, but were unable to offer from these findings why such an exchange occurred. Meigs demonstrated by the injection of carbon into the abdominal cavity containing ascitic fluid its rapid passage into the pleural cavity. He believes that the transmission is through lymphatic drainage.

In six cases of cirrhosis of the liver, and in five cases of ascites due to malignant implants on the peritoneal surfaces, fluid was present in the left hemithorax.

In many of the fluids in the abdomen due to a cardiac condition, fluid was present in the left hemithorax as well as in the right. Recently, McPeak and Levine have called attention to the ratio of this finding. Depending on the method considered, right hydrothorax predominated in from 56 to 89 per cent of cases and left hydrothorax in from 12 to 17 per cent. Fluid was equally distributed in 3 to 27 per cent.

### *Analysis of Cases with Fluid in the Pleural Cavity*

By the performance of these taps we were impressed by the number of times we were able to demonstrate fluid in the left hemithorax with a minimal presence of physical signs. We found

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TABLE 1

#### ETIOLOGY OF PLEURAL FLUIDS OTHER THAN TUMOR

Arteriosclerotic Heart Disease	15
Tuberculosis	6
Rheumatic Heart Disease	6
Cirrhosis	3
Pneumonia	2
Post Operative Embolus	2
Nephritis	2

*One Each* Lupus Erythematosus, Ovarian Cyst, Post-Operative Effusion, Hemolytic Anemia, Over-Hydration, Chronic Lung Disease

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the x-ray findings of limited value Sante called attention to the difficulty in the interpretation of basal exudates of subphrenic origin by x-ray film

In this group of patients, we had 9 cases of cirrhosis of the liver, 3 of which were proven by postmortem, 6 proven clinically, with a maximum amount of their symptoms and signs abdominal in nature, but in three of whom pleural fluid was present in both the left pleural cavity and abdominal cavity, and demonstrated the fluid transmission sign An analysis of these fluids for their cellular contents failed to reveal the presence of any cells that could be considered malignant In 21 cases we were able to secure positive pleural cellular findings, proven by surgery and biopsy in 13, and by the clinical course in 8

TABLE 2  
PLEURAL SEROSAL IMPLANTS WITH EFFUSION

S O U R C E	
Breast	2
Gallbladder	1
Lung	1
Leucosarcoma	1

In one of these, the case of leucosarcoma, findings in the effusion made the diagnosis unaided

In breaking down our figures to show the types of tumor, the following is the result

TABLE 3  
TYPES OF TUMORS

	No. of Cases	Tumor Cells Found
Primary Carcinoma of Lung	22	9 (40%)
Carcinoma of the Breast	16	4 (25%)
Lymphosarcoma of Lung	8	4 (50%)

### SUMMARY

1) In all cases of pleurisy with effusion the etiological factor of an abdominal lesion must be considered

2) Small amounts of fluid may be present in either pleural cavity, and may be demonstrable only by physical signs and exploratory aspiration

3) In a group of abdominal and thoracic taps, using a size 16 to 18 gauge 1½ to 2 inch needle, straight or short bevel, we have had no untoward reactions, either local or general

4) Five to ten cc of fluid are adequate to demonstrate the presence of pathological cells

5) The importance of the presence of fluid in the thoracic cavity with a nonmalignant mass in the abdomen must be emphasized

6) The x-ray may show only a haziness at either base which is difficult to distinguish between a small amount of fluid, atelectasis, or pulmonary congestion, and aspiration may be the only method of proving the presence of effusion

7) It is exceedingly rare for an inflammatory lesion in the chest to pass downwards through the diaphragm and involve the abdominal cavity

8) We have presented a case of a Meigs' syndrome

9) The increasing number of returned veterans with amebiasis involving the liver makes it necessary for us to remember it as an etiological factor of pleural effusion

10) The gastroenterologist must carefully examine the thoracic cavity in many diseases involving the abdominal organs

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We are grateful to Dr Dorothy Nagel Shaver, Dr Charles F Becker and Dr Kornel Terplan for permission to use their pathological findings and to Dr Joseph E Macmanus for report on Amoebiasis case

### RESUMEN

1) En todo caso de pleuresia con derrame se debe considerar el factor etiológico de una lesión abdominal

2) Pueden ocurrir pequeñas cantidades de líquido en cualquiera cavidad pleural y es posible demostrar su presencia solamente mediante los signos físicos y la punción exploratoria

3) En un grupo de paracentesis abdominales y torácicas en las que se emplearon agujas de calibre 16 a 18, de 1½ a 2 pulgadas de largo, no se observaron reacciones contraproducentes, ni locales ni sistémicas

4) De cinco a diez cc de líquido son suficientes para demostrar la presencia de células patológicas

5) Se debe recalcar la importancia de la presencia de derrame en la cavidad torácica con un tumor abdominal no maligno

6) Es posible que la radiografía solamente muestre una leve sombra en una de las dos bases, la que es difícil de distinguir entre un derrame pequeño, atelectasia o congestión pulmonar, y la paracentesis puede ser el único método de comprobar la presencia de derrame

7) Es sumamente raro que una lesión torácica inflamatoria pase a través del diafragma e invada la cavidad abdominal

8) Hemos presentado un caso de síndrome de Meigs

9) El número creciente de veteranos de la guerra que han re-

gresado con amibiasis que afecta al hígado nos obliga a recordar que este es un factor etiológico de derrames pleurales

10) El gastroenterólogo debe examinar cuidadosamente la cavidad torácica en muchas enfermedades que afectan los órganos abdominales

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# Tuberculous Infection in the Children of Lima, Peru\*

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The high figures of tuberculous infection found in Peru during the last 10 years, in which tuberculosis control in the various communities has been carried out, almost systematically, has shown that our country is passing through a stage of mass infection of tuberculosis

The investigation, with the purpose of determining the percentage of infection, as well as tuberculosis morbidity, have given figures of infection that fluctuate between 30 and 60 per cent in the first six months of life and 70 to 80 per cent in the adults

By means of the intra-dermal reaction of Mantoux with 1/1000 and 1/100 old tuberculin of Koch, in more than 100,000 individuals in the Capital of Peru from 1936 to 1946, the following results have been obtained

Out of 50,000 children from 0 to 6 months of age, 25 per cent of infection was obtained in the first month, and 66 per cent in the sixth month, of 10,000 children from 7 to 12 months, 50 per cent reaction to tuberculin was obtained, of 20,000 children from 1 to 5 years, 60 per cent was obtained, of 10,000 children from 6 to 15 years, 65 per cent was obtained, and of 15,000 children over 15 years, 70 per cent reaction to tuberculin was obtained

We have tried to find the cause for the high percentage of tuberculous infection during the first six months of life among the children of Lima We have reached the conclusion that it is due to the lack of systematic examination of the pregnant women, to the lack of special services in the hospitals in order to separate tuberculous patients, to the lack of special services for the separation of the newborn of infected mothers, and to the need of establishing a methodical form of vaccination of the newborn with B C G

Bearing these facts in mind, we have procured the above mentioned services Through our suggestions, a special service for pregnant in our Maternity Hospital of Lima has been established We are having systematic control of pregnant women by means of x-ray films Finally, due to our initiative too, the first hospital for the newborn of infected mothers was just inaugurated This

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hospital is located in the town of Chosica, 40 Km from Lima, 900 m above sea level. All the children of infected mothers, that are born in the Maternity Hospital, after being vaccinated by BCG are sent to this hospital in Chosica.

This work was carried out with the cooperation of the Ministry of Public Health, the Head of the National Antituberculosis Campaign, and the Rotary Club of Lima. We believe this is going to be useful in order to cut down, in a short time, the percentage of infection found in the infants of Lima.

The prevalent concept in my country is that the antituberculosis campaign must begin with the periodical x-ray examination of the pregnant, must follow immediately after birth with the separation of the infected mother, and BCG vaccination. Thus, my country expects to reduce the high levels of infection, morbidity and mortality caused by tuberculosis in infants.

Before finishing, I would like to mention the need for establishing a standard procedure in the kind of tuberculin to be used in testing and determination of rates of infection in all countries, starting with the Panamerican nations. Also, a standard must be set upon the dilutions of tuberculin that is to be used, so it will be possible to make comparison of the results and investigations in every place.

On my part, I may suggest the use of the old tuberculin of Koch. Results obtained in a work were presented at the Tenth Latin American Congress of Tuberculosis, held at Buenos Aires in 1940. We made a comparative study of the degree of intensity to the tuberculin reaction, injecting old tuberculin of Koch in the dermis of the forearm, and P.P.D. in the other forearm of the same person, of the same dilutions. We proved better results, more positive reactions in tests with old tuberculin. These tests were done in more than 2,000 school children between 6 and 15 years of age.

It is equally important to set a standard pattern of the dilutions to be used. We consider that it would be enough to use dilutions 1/1000 and 1/100 by the technique of Mantoux. To the negative cases with 1/1000, a new injection is given with 1/100. Those who are negative to this dilution could be considered as free of infection.

### SUMMARY

The author has done more than 100,000 tuberculin tests in order to ascertain the incidence of tuberculous infection, at a different age of life. He has found 66 per cent infection at the sixth month of life, 60 per cent at the fifth year, and from 70 to 80 per cent in the adult.

The reason for the high percentage found in the first six months of life lies in the lack of special services for infected pregnant women and in the lack of systematic x-ray examination of all pregnant. The institution of such methods and services, the establishment of hospitals for the separation of the new born, previously B C G vaccinated, of the infected mother, are going to aid in the lowering of the high levels of infection, morbidity and mortality, due to tuberculosis, in infancy.

Standardization of tuberculin to be used in the determination of the degrees of tuberculosis infection as well as conventional dilutions are advocated.

### RESUMEN

El autor ha llevado a cabo más de 100,000 pruebas a la tuberculina a fin de verificar la frecuencia de la infección tuberculosa en diferentes edades de la vida. Ha encontrado un 66 por ciento de infección en el sexto mes de vida, 60 por ciento en el quinto año y de 70 a 80 por ciento en el adulto.

La razón del alto porcentaje encontrado en los primeros seis meses de vida se halla en la falta de servicios especiales para mujeres preñadas infectadas y la falta de exámenes radiográficos sistemáticos de todas las mujeres embarazadas. La institución de esos métodos y servicios y el establecimiento de hospitales para la separación del recién nacido, previamente vacunado con B C G, de la madre infectada, van a ayudar a bajar los elevados niveles de la infección, morbilidad y mortalidad por tuberculosis en la infancia.

Se aboga por la normalización de la tuberculina que se va a usar en la determinación de los grados de infección tuberculosa, y por el empleo de diluciones convencionales.

# Pneumoperitoneum and Phreniclasia in the Treatment of Pulmonary Tuberculosis

## Therapeutic Observations in 550 White and Negro Cases\*

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### *Introduction*

During World War II many discharged soldiers and sailors were received in the United States Veterans Hospital at Oteen, North Carolina, with pulmonary tuberculosis. A large number of these patients were in the younger age group, and unfortunately had extensive bilateral disease, many with cavitation. In the past, the only treatment which could be offered a patient with this amount of disease was bed rest. This presented a serious problem.

It was decided in 1943 to treat this type of case with a phreniclasia on the side most involved, and to follow this with pneumoperitoneum. If both lungs were equally involved, pneumoperitoneum was instituted and the phreniclasia added later on the side with the least lift of the diaphragm. Results were so encouraging, that the treatment was gradually applied in more favorable cases. This article reviews 550 cases treated and endeavors to assay the value of this method of treatment.

In evaluating the statistical data, it is important to bear in mind the fact that the majority of patients in this series had far advanced pulmonary tuberculosis, many with a poor prognosis. It is realized that the time element is very important in evaluating any form of pulmonary collapse, and we therefore feel justified in dividing the cases into two groups, one group having the treatment six months or more, and the other six months or less.

### *Physiology*

Normally, the general pressure within the abdomen tends to equal that of the atmosphere. The subdiaphragmatic region, however, differs from other parts of the abdominal cavity in that the intrapleural negative pressure is transmitted to this area. As

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this subatmospheric pressure in the upper abdomen is gradually changed to a positive pressure by the intraperitoneally injected air, there is an upward pulling force exerted by the intrapleural negative pressure and the diaphragm rises. The elevation of the diaphragm is also influenced by the lifting effect of the air injected.

With the rise of the diaphragm the thoracic capacity is reduced, and the intrapleural negative pressure becomes less negative. This latter change permits a greater contraction of the elastic structures of the lung, and pulmonary relaxation is attained. We see, therefore, that when a phreniclasia and pneumoperitoneum have been instituted, two things are accomplished: first, the high rise of the diaphragm reduces the lung volume and facilitates drainage; second, there is marked relaxation of the lung and bronchial tree. There is little shortening of the bronchi and little narrowing of their lumina during expiration, and this allows for continuous drainage through patent bronchi. Improved drainage and relaxation of the lung are the two outstanding factors which contribute to the excellent results secured in healing the lung with pneumoperitoneum.

Every patient in this series has been asked the question, "What did you notice after the treatment was started?" A common reply was, "My cough and sputum increased in the beginning but it was easier to raise the sputum." Favorable symptomatic response was noted early in nearly all cases. Expectoration was easier and the cough and sputum gradually disappeared. Improvement in pulmonary drainage was followed by a decrease in toxicity and a gradual disappearance of constitutional symptoms, the temperature and pulse returned to normal, the patient began to sleep at night, his appetite improved, and he started to gain in weight.

### *Indications*

1) Phreniclasia and pneumoperitoneum are indicated when the tuberculous lesion is too extensive for bilateral pneumothorax. Patients with extensive bilateral disease, for whom nothing can be offered in the form of surgical procedures, not only secure considerable relief, but in many instances attain a clinical cure.

2) Cases with unsatisfactory collapse of the lung with pneumothorax due to adhesions where a pneumonolysis has been unsuccessful. In these cases the lung has been reexpanded and a phreniclasia and pneumoperitoneum added with favorable results.

3) Pulmonary hemorrhage which can not be controlled by artificial pneumothorax.

4) As a measure to prepare patients for thoracic surgery, who are at the time too ill for radical intervention. Many cases with

scattered pulmonary infiltrations below the cavity area can be cleared up completely, and the apical cavities so reduced in size that thoracoplasty becomes feasible and its extent reduced

5) Pneumoperitoneum is indicated as an adjunct to thoracoplasty when lesions in the lower portions of the lung remain active, or a new focus develops in the contralateral side

6) Pneumoperitoneum alone without phreniclasia is the treatment of choice in cases of tuberculous pneumonia Spontaneous collapse and the danger of empyema make pneumothorax a dangerous procedure

7) To help obliterate the pleural space in pneumothorax cases when, following discontinuance of the treatment, the treated lung fails to reexpand completely

8) The treatment of pulmonary tuberculosis in the diabetic patient The predominantly exudative and caseous lesions which exist in these cases and the frequency of spontaneous collapse during pneumothorax treatment make pneumoperitoneum the treatment of choice

9) In severe intractable cough Severe cough which produces physical exhaustion, loss of appetite, vomiting and disturbed rest is relieved Pneumoperitoneum in these cases is a palliative and justified therapeutic measure

10) Mid zone cavities, which do not respond to pneumothorax, frequently close with pneumoperitoneum

### *Complications*

Complications in this series have been surprisingly few and there have been no accidental deaths The most serious complication is air embolism, but we have not experienced it in any of our cases Another complication is the passage of air through the aortic or esophageal hiatus up through the mediastinum into the fascial planes of the neck This occurred in one case Subsequent treatment was to reduce the amount of air refill and lower the intraabdominal pressure Treatment has been continued and the complication has not recurred

Three patients in this series developed appendicitis and were operated upon successfully There was no evidence of chronic peritonitis attributable to the treatment The incidence of acute appendicitis in patients treated with pneumoperitoneum does not appear to be any higher than in the rest of the sanatorium cases Two patients developed peritoneal effusions to a degree requiring aspiration, and treatment with pneumoperitoneum was discontinued Small asymptomatic effusions were noticed in five cases but these did not interfere with continuance of the treatment

They were seen to occupy the space between the liver and the lateral abdominal wall when roentgenologic examination was made with the patient in the upright position. Occasionally an effusion may be seen in the space between the stomach and the lateral abdominal wall. Care must be exercised not to mistake this for a fluid level in the stomach.

Peritoneal adhesions were seen in a number of cases but in the majority caused no trouble. In some instances, however, they will prevent a satisfactory rise of the diaphragm, and in six of our cases pneumoperitoneum had to be discontinued as unsatisfactory.

Subcutaneous emphysema during pneumoperitoneum treatment has occurred but is a complication of minor importance. Its chief symptoms are localized pain and palpable crepitation. The resulting discomfort is slight and disappears in a short time. The cause is generally a faulty position of the needle and the injection of air into the abdominal wall instead of the peritoneal cavity. Improved technique by the operator should eliminate this complication entirely.

After the induction of pneumoperitoneum, the patient may complain of pain in the hypochondriac or epigastric area and a referred pain along the phrenic nerve into the neck and outward to the shoulder. If this occurs, we have found it not severe, and it generally does not recur after the first treatment.

Penetration of the intestine or abdominal organs has not occurred to our knowledge. This complication should never arise if ordinary care is practiced.

### *Technique*

The procedure of initiating pneumoperitoneum and giving re-fills is not difficult and is believed to be much less dangerous than pneumothorax. Following the phreniclasia, we wait three weeks to allow the patient to become adjusted to his temporary phrenic interruption. In selecting the point of entry the proximity of surgical scars should be avoided because of the possibility of intestinal loops being adherent to the abdominal wall. We have selected a routine site to the left of the umbilicus through the rectus muscle. It is felt that the rectus forms a muscular valve and prevents subcutaneous emphysema, especially in patients with considerable cough.

The procedure is carried out with the patient lying flat on his back. The skin is sterilized with tincture of merthiolate, and with strictly aseptic technique the skin and various layers of the abdominal wall are infiltrated with one per cent plain novocain, using a 25 gauge, 1½ inch needle. After adequate anesthesia is secured, a 19 gauge, 3 inch needle is inserted. In the beginning

of the treatment it is advisable to attach a syringe filled with novocain to the needle, and a free flow of novocain from the syringe is a good indication that the needle has reached the free peritoneal space. By using novocain one can avoid the possibility of air embolism. With reference to the latter, it is advisable to draw back on the plunger of the syringe before injecting any air to make sure that the point of the needle is not in a blood vessel. The air is then introduced by means of a Zavod pneumothorax apparatus, which we have found to be the most satisfactory for this type of treatment.

The initial treatment is 450 cc of air repeated twice weekly for two weeks. This is a trial period to determine how the patient adjusts to the treatment, if it is satisfactory, he is placed on a weekly schedule, and the amount of air refill is gradually increased. The maximum amount of air given at a refill to the average patient, after the pneumoperitoneum is well established, is 900 cc of air. We endeavor to build up the pressure in the abdomen to a positive pressure of 10 cm of water and secure a lift of the diaphragm to the anterior third rib. Cases in which this can be accomplished secure the best results. Some patients can not tolerate this pressure, and the best policy to follow is the amount of air injected should be gauged on the basis of individual requirements and subjective response of the patient during treatment.

There are certain symptoms and signs which can be used as indicators of a successful induction of pneumoperitoneum, these are referred pain along the phrenic nerve into the neck and outward to the shoulder, and a feeling of tightness in the hypochondriac or epigastric area. The objective signs are disappearance of liver dullness and the presence of a tympanic percussion note. Under fluoroscopy one will note the beginning lift of the diaphragm by the air beneath.

Following the initial treatment, the patient is requested to lie flat on his back until bed time. In a few cases the pain was severe and was relieved by elevating the foot of the bed. The patient is also advised to turn over in bed slowly or he will notice a sudden shifting or rolling of the air and an uncomfortable feeling will result, this disappears as the intraabdominal pressure is increased and the pneumoperitoneum becomes well established.

One of the most frequent causes of failure to induce a pneumoperitoneum is failure to insert the needle in far enough. If the point of the needle does not reach the abdominal cavity but is lying in the tissues, the flow of air is very slow and the manometer will show a non-oscillating positive pressure of +15 to +25 cm of water, and the patient will generally complain of pain at the site of injection.

### *Report of Cases*

New cases on admission to the hospital are reviewed by a Therapy Board, after a thorough study and examination on the Reception Service. This Board is composed of the Clinical Director, Chiefs of the Surgical, Medical and X-ray Services and the Ward Surgeon. This plan gives the patient the benefit of the knowledge of a group well trained in the treatment of tuberculosis, and eliminates the error of individual judgment. All cases are routinely reviewed by the above Board every three months, with new x-ray films and sputum examinations, or sooner if conditions arise requiring the Board's opinion.

In this review the Therapy Board's opinion of the status of the case forms the basis of this study. Table I lists what has occurred in the 550 cases treated, there are 410 cases still under treatment, 45 prepared for major surgery, 50 discontinued as unsatisfactory and 45 dead.

The 410 cases still under treatment have been divided into white and negro groups treated six months or more and six months or less. Table II shows 134 white cases with far advanced pulmonary tuberculosis treated six months or more. The sputum has been converted in 106 or 79 per cent. Cavity closure occurred in 80 of 111 cases with cavitation, or 72 per cent. The clinical status of this group finds 14 arrested, 2 apparently arrested, 35 quiescent, 70 improved, and 13 unimproved. In the group listed as improved there has been clearing of the pulmonary lesions, cavities reduced in size or closed, and toxicity relieved. In the second section of Table II we find 18 moderately advanced cases. The sputum has been converted in 16 or 89 per cent. Cavities closed in 10 of 11 cases with cavitation, or 91 per cent. The clinical status reveals 4 arrested, 4 quiescent, 8 improved, and 2 unimproved.

Table III reviews the results attained in 76 far advanced and 6 moderately advanced negro patients treated 6 months or more. In the far advanced group of 76 the sputum was converted in 56 or 73 per cent, cavity closure occurred in 37 of 55 cases with cavitation, or 67 per cent. The clinical status finds 3 arrested, one apparently arrested, 33 quiescent, 29 improved, and 10 unimproved. In the six moderately advanced cases sputum conversion and

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TABLE I  
Classification of 550 Cases Treated with  
Phreniclasia and Pneumoperitoneum

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No. of Cases	Still Under Treatment	Prepared for Major Surgery	Discontinued as Unsatisfactory	Expired
550	410	45	50	45

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T A B L E 2  
FAR ADVANCED WHITE CASES

Time Under Treatment	No of Cases	Sputum Positive	Sputum Converted	Cavities		Cavities Closed		C L I N I C A L				S T A T U S		
				Open	Closed	Arrested	Apparently Arrested	Quiescent	Improved	Unimproved				
6 months	20	20	13	5	9			4	15	1				
6 to 12 months	54	54	40	16	27		1	13	33	7				
12 to 18 months	28	28	24	6	20	4	1	7	13	3				
18 to 24 months	17	17	16	2	11	4		7	5	1				
24 to 30 months	13	13	11	2	12	4		4	4	1				
30 to 36 months	2	2	2		1	2								
TOTAL	134	134	106	31	80	14	2	35	70	13				

MODERATELY ADVANCED WHITE CASES

6 months	3	3	3		3				3					
6 to 12 months	8	8	6	1	3	1		3	2	2				
12 to 18 months	3	3	3		2	1			2					
18 to 24 months	2	2	2		1	1			1					
24 to 30 months	2	2	2		1	1		1						
30 to 36 months														
TOTAL	18	18	16	1	10	4		4	8	2				

## T A B L E 3

## FAR ADVANCED NEGRO CASES

Time Under Treatment	No of Cases	Sputum Positive	Sputum Converted	Cavities		Cavities Closed	C L I N I C A L S T A T U S			
				Open	Closed		Arrested	Apparently Arrested	Quiescent	Improved Unimproved
6 months	11	11	6	2	1				1	9 1
6 to 12 months	35	35	23	12	21				14	15 6
12 to 18 months	14	14	12	3	4				9	3 2
18 to 24 months	10	10	9	1	9		1	1	5	2 1
24 to 30 months	3	3	3		1		1		2	
30 to 36 months	3	3	3		1		1		2	
TOTAL	76	76	56	18	37		3	1	33	29 10

## MODERATELY ADVANCED NEGRO CASES

6 months										
6 to 12 months	2	2	2		1				2	
12 to 18 months	3	3	3		3				3	
18 to 24 months	1	1	1		1				1	
24 to 30 months										
30 to 36 months										
TOTAL	6	6	6		5				6	

T A B L E 4  
FAR ADVANCED WHITE CASES

Time Under Treatment	No of Cases	Sputum Positive	Sputum Converted	C A V I T I E S		C L I N I C A L S T A T U S				
				Open	Closed	Arrested	Apparently Arrested	Quiescent	Improved	Unimproved
Less than 6 mos	107	107	45	69	18			1	77	29

FAR ADVANCED NEGRO CASES

Less than 6 mos	44	44	20	19	9				33	11
TOTAL	151	151	65	88	27			1	110	40

MODERATELY ADVANCED WHITE CASES

Less than 6 mos	15	15	9	7	4				14	1
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MODERATELY ADVANCED NEGRO CASES

Less than 6 mos	10	10	9	2				2	7	1
TOTAL	25	25	18	9	4			2	21	2



cavity closure in 5 cases with cavitation was 100 per cent All six cases at present are in the quiescent stage

In this review one may be questioned in presenting the group in Table IV We realize that the time element is very important in evaluating any form of pulmonary collapse, and many of these cases have had the treatment for only two or three months In analyzing the table, however, and noting the percentage of sputum conversions and cavity closure, their review seems justified

There are 151 white and negro cases with far advanced disease Sputum conversion occurred in 65, or 43 per cent and cavity closure in 27 of 115 cases with cavitation, or 23 per cent In the moderately advanced group of 25 treated less than 6 months, 18 converted their sputum, or 72 per cent, cavity closure occurred in 4 of 13 cases with cavitation, or 31 per cent

Sputum studies have been by the concentrate method of 72-hour specimens If the sputum is found negative, a culture or guinea pig inoculation is done Examination of gastric washings is done if a satisfactory sputum specimen can not be obtained Cavity closure is confirmed by planigraphic study if any question arises in the interpretation of the chest x-ray film

One of the indications for pneumoperitoneum is to prepare the patient for major surgery Forty-two cases with extensive disease showed such remarkable improvement that thoracoplasty could be done for residual thick-walled cavities at the apex One lobectomy was done for a mid-zone cavity on the right Two lucite packs were inserted for residual cavities at the apex, the patients refusing thoracoplasty

In the group of 50 cases discontinued as unsatisfactory, 31 were white and 19 negro This seems a rather large number and probably indicates an error in judgment in selection of cases to be treated All were in the far advanced group, prognosis was poor, and any type of collapse therapy was probably not indicated Extension of disease under treatment was the cause of discontinuing it in 31 cases Other conditions and complications developed in 19 cases and influenced the decision to discontinue treatment Failure of the diaphragm to rise because of adhesions was the cause in 6 cases Severe intestinal tuberculosis developed in 2 cases Tuberculosis of the spine, intestinal obstruction and amyloidosis accounted for 3 cases Two cases had severe endobronchial disease and dyspnea One of these patients was placed on streptomycin therapy and has improved Two patients developed a large amount of abdominal fluid, obliterative peritonitis developed, and refills became difficult to give One of these cases had reached the quiescent stage at the time the fluid appeared One patient, in whom treatment was discontinued as unsatisfactory, had rectal

and scrotal tuberculous sinuses and progressive pulmonary disease. He was placed on bed rest, streptomycin, and a fistulectomy was done. At the present time all sinuses are closed, his sputum is negative, and he is classified as quiescent.

In the group of 45 fatal cases, 26 were white and 19 negro. In 43, the cause of death was extensive pulmonary tuberculosis. One patient died of coronary occlusion, phlebothrombosis of the left leg and pulmonary embolism. A pericardial effusion developed in one case. A pericardial tap was done and the fluid on examination revealed tubercle bacilli.

The 410 cases still under treatment have been classified as to age. In the age group of 20 to 30 years we find 235 cases, 89 in the group 30 to 40 years, 40 in the group 40 to 50 years, and 46 in the oldest age group of 50 to 60 years.

Phreniclasia was successfully done on the right in 194 cases and on the left in 166. There were 116 unsatisfactory pneumothoraces discontinued and the lungs reexpanded. Pneumoperitoneum was then instituted with satisfactory results. Pneumoperitoneum was given in combination with pneumothorax in 7 cases, and in 10 cases with thoracoplasty completed pneumoperitoneum was added to control a spread to the contralateral side. There were 76 cases found with endobronchial tuberculosis. This condition was treated with the application of 30 per cent silver nitrate and the pneumoperitoneum continued.

### *Discussion*

The ultimate aim of any form of treatment is to aid in the recovery of the patient, and after reviewing the results obtained in this series, we are convinced that pneumoperitoneum is of great value in the treatment of pulmonary tuberculosis. It should not be considered a method of treatment to replace all other types of collapse therapy, but another procedure to be used by the physician in selected cases. Ill-chosen or indiscriminate administration of the procedure is bound to discredit the treatment.

In properly selected cases, pneumoperitoneum, when given at regular intervals, is capable of inducing good drainage and relaxation of the lung. These two outstanding factors are the reasons for the excellent results seen in this series. This therapy appears most logical in the treatment of bilateral disease, although the selection of more favorable cases found the results more impressive. We have found this method of treatment capable of effecting a cure in many patients who unquestionably were not suitable for either pneumothorax or thoracoplasty. The procedure has also made suitable for thoracoplasty a considerable number of cases not likely to become so without some form of preliminary collapse.

If indications for pneumothorax are present, we feel that this type of collapse should be instituted. The use of pneumoperitoneum, however, has the following advantages over the use of artificial pneumothorax:

1) The disease in the lungs can be observed at all times by fluoroscopy and roentgenography and its response to therapy. This cannot be done in a large percentage of pneumothorax cases, since the diseased portion is so collapsed that it cannot be followed without reexpansion.

2) The complications are extremely few. Thickened pleura, spontaneous collapse, empyema, and non-expandable lungs are seldom seen.

3) Pneumoperitoneum may be discontinued or continued again far more readily than artificial pneumothorax.

4) Pneumoperitoneum treats bilateral disease at the same time, providing a great saving of time to both patient and physician.

The treatment of pulmonary tuberculosis with pneumoperitoneum is going through the same stages as experienced with pneumothorax. There is a tendency to give too large refills as was done in the early days of pneumothorax therapy. We are endeavoring to secure the maximum lift of the diaphragm, and excessive refills merely depress the abdominal contents downward and toward the spine, and the patient is made uncomfortable. In our experience, the average refill after the pneumoperitoneum is well established should be 900 cc of air weekly, and the intra-abdominal pressure built up to a positive pressure of 10 cm of water. Cases with a lift of the diaphragm to the anterior third rib secure the best result.

Pneumothorax therapy in the treatment of pulmonary tuberculosis in the negro has been unsatisfactory in this hospital. Complications have resulted, though the cases have been handled carefully with frequent small refills, and the patient given the benefit of early pneumonolysis if adhesions were present. In acute bilateral disease the introduction of pneumoperitoneum has produced excellent results. In the past, disease of this type in the negro has been looked upon as fatal, and such a result could not have been obtained by any other method of collapse therapy at our disposal. We feel that pneumoperitoneum is the treatment of choice in the negro.

Following the termination of collapse there is a maximum and satisfactory restoration of the normal lung volume and function provided a permanent paralysis of the hemidiaphragm has not occurred. When treatment is terminated, refills are simply discontinued, and no undesirable effects have been observed.

The criteria upon which we must base our appraisal of the value

of pneumoperitoneum is its ability to close cavities, convert the sputum and heal the lung with a minimum of serious complications. We have tried it in a large series of white and negro cases and find that it meets this criterion.

### SUMMARY

1) A therapeutic review of 550 patients with pulmonary tuberculosis, treated by a combination of temporary phrenic nerve interruption and pneumoperitoneum, has been presented.

2) The physiology, indications, and complications have been stated.

3) The technique of the procedure of pneumoperitoneum has been outlined.

4) It is of value in preparing the patient for thoracoplasty.

5) This method of treatment is capable of effecting a cure in many cases which unquestionably are not suitable either for pneumothorax or thoracoplasty.

6) Cavity closure occurs equally as well at the apex as in the basal portion of the lung.

7) In 134 far advanced white patients treated for six months or more, 106, or 79 per cent converted their sputum. Cavity closure occurred in 80 cases, or 72 per cent. In the far advanced 76 negro patients, 56 or 73 per cent converted their sputum, cavity closure occurred in 37, or 67 per cent. In the more favorably selected cases, the results were more impressive.

8) The duration of treatment parallels that required by other types of collapse therapy.

9) The importance of maximum elevation of the diaphragm is emphasized.

10) Artificial pneumoperitoneum combined with phrenic crush has been found a valuable treatment, it avoids the serious complications of artificial pneumothorax and gives to many patients, hopelessly ill, their chance to recover.

### RESUMEN

1) Se ha presentado un repaso terapéutico de 550 tuberculosos pulmonares tratados mediante la combinación de la interrupción temporal del nervio frenico y neumoperitoneo.

2) Se han expuesto la fisiología, las indicaciones y las complicaciones.

3) Se ha bosquejado la técnica del neumoperitoneo.

4) Es valioso para preparar al paciente para la toracoplastia.

5) Este método de tratamiento es capaz de efectuar curaciones en muchos casos que indudablemente no son apropiados para el neumotórax o la toracoplastia.

6) Cierres de cavernas tienen lugar igualmente bien en el vértice o en la zona basal del pulmón

7) En 134 pacientes blancos muy avanzados, tratados por seis meses o mas, en 106, el 79 por ciento, se convirtió el esputo Cierre de cavernas ocurrió en 80 casos, o sea en el 72 por ciento En los 76 pacientes negros muy avanzados, en 56, el 73 por ciento, se convirtió el esputo, cierre de cavernas ocurrió en 37, o en el 67 por ciento En los casos seleccionados más favorablemente los resultados fueron aun más imponentes

8) La duración del tratamiento paralela el requerido en otros tipos de colapsoterapia

9) Se hace hincapié sobre la importancia de obtener la elevación máxima del diafragma

10) Se ha encontrado que el neumoperitoneo artificial combinado con la trituración del frénico es un tratamiento valioso que evita las graves complicaciones del neumotórax artificial y que les ofrece a muchos pacientes desesperanzados la oportunidad de recobrar la salud

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## D I S C U S S I O N

LEON H HIRSH, MD, FCCP

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I should like to compliment Dr Moyer on the excellence and the completeness of his study

Pneumoperitoneum has justly assumed its place in our armamentarium against tuberculosis I have been using therapeutic pneumoperitoneum for the past ten years With reference to the safety and simplicity of the procedure, I wish to mention that I have established pneumoperitoneum in my office Also, patients who have been discharged from the sanatorium are maintained as ambulatory pneumoperitoneum subjects in the office, and present no greater problem than those receiving ambulatory pneumothorax treatment

Concerning the site of injection of the air, I prefer to introduce the initial and a few subsequent inflations in the left lower quadrant of the abdomen However, when there is an adequate rise of the diaphragm, I usually choose a site through the lower thorax I do not insist on the attainment of a set positive pressure I prefer to gauge the amount of air according to the position of the diaphragm and the reaction of the patient For subjective reasons on the part of the patient, it is expedient to use local anaesthesia for each refill

I have found it advantageous and entirely safe to have an

assistant attach a rubber bulb to the distal bottle of a Robinson pneumothorax apparatus and pump the air into the peritoneal cavity rather rapidly

I should like to add the following to Dr Moyer's list of indications for pneumoperitoneum in pulmonary tuberculosis (1) Patients following childbirth are likely to suffer with exacerbation of their pulmonary lesions Here, pneumoperitoneum, when induced after delivery, maintains the diaphragm at the high level of the last trimester of pregnancy, and continues the pulmonary relaxation which would otherwise be lost (2) Elderly individuals who are not good bilateral pneumothorax prospects will often do well with pneumoperitoneum provided there is no severe cardiovascular impairment (3) Patients who have tuberculous enterocolitis in addition to pulmonary lesions will obtain multiple benefits from this procedure (4) Individuals who suffer with thoracic pain due to basal diaphragmatic adhesions will enjoy some relief with pneumoperitoneum

As Dr Moyer has said, one may anticipate good results from therapeutic pneumoperitoneum only if it is employed in critically selected instances Then one should allow a sufficient length of time to achieve healing and recovery with the use of this measure Consider the time of healing in the natural reparative processes of tuberculosis—particularly that type which is selective for pneumoperitoneum Patients who have had thoracoplasty may not be expected to convert their sputum in possibly one to two years, and even many continue under the classification of "maximum benefit" One is not justified, therefore, in discontinuing artificial pneumoperitoneum if conclusive therapeutic results, roentgenologic or bacteriologic, are not accomplished in two or three months This commentary does not apply to the study just presented However, with the prevailing views toward short term pneumothorax there is a popular tendency to evaluate pneumoperitoneum in the same light While the fundamental biologic processes are similar, I feel that by the very nature of the type of disease selected for artificial pneumoperitoneum one should not expect dramatic therapeutic response in too short a time

There is another point of importance which I wish to mention It is well known that following reexpansion of the lung after artificial pneumothorax there remains in most instances some degree of functional impairment of the previously relaxed lung due to plural changes Since pneumoperitoneum does not influence the pleurae, this treatment is free of the liability of producing a post-therapeutic pulmonary insufficiency

I wish to congratulate Dr Moyer again on his splendid presentation of this very important subject

## D I S C U S S I O N

JACOB J MENDELSON, MD, FCCP  
Chicago, Illinois

The controversial aspects of pneumoperitoneum with phreniclasia in the treatment of chronic pulmonary tuberculosis are in a great measure clarified by Dr Moyer's interesting and instructive presentation. His wealth of clinical material and his striking portrayal of the subject offers convincing testimony in support of his conclusion that there are definite indications for this type of collapse therapy.

Based upon Dr Banyai's studies on the subject we have employed pneumoperitoneum with phreniclasia in selected cases over a period of several years with clinical observations similar to those presented by Dr Moyer. Pneumoperitoneum often aids the action of phrenic nerve paralysis and favorable results have been noted in apical cavities as well as in lesions of the lower lobes. In the treatment of tension cavities where artificial pneumothorax is inapplicable or unsatisfactory the percentage of closure following pneumoperitoneum with phrenic paralysis compares favorably with those obtained with the more radical methods of collapse therapy.

The following case demonstrates the possibilities of this type of treatment. This patient, age 47 was admitted to Fox River Sanitarium in 1942 with a diagnosis of far advanced pulmonary tuberculosis complicated by tuberculous enteritis. His sputum was positive for tubercle bacilli. Figure 1 shows a tension cavity de-

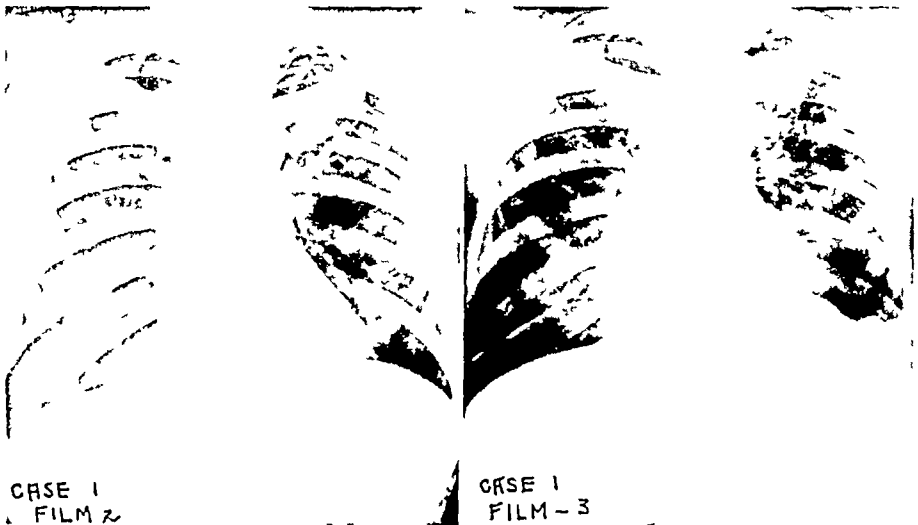


FIGURE 1

FIGURE 2

veloping during the course of pneumothorax treatment Pneumothorax was discontinued and Figure 2 reveals closure of the cavity following phreniclasia with pneumoperitoneum He is now an arrested case and is employed eight hours a day as a salesman

Dr Moyer should be complimented for his valuable contribution to the progress of tuberculosis therapy It has been a privilege to discuss his excellent paper



# Differential Diagnosis and Treatment of Congenital Cystic Malformation of the Lung\*

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Congenital cystic malformation of the lung presents an interesting and difficult problem in differential diagnosis since the clinical picture frequently is very similar to that produced by a number of other conditions within the thorax. Pulmonary cystic lesions may be of two types—congenital and acquired. This paper has to deal only with the former type.

The symptomatology produced by congenital malformation of the lung is brought about by one of two mechanisms, i.e. (1) disturbance of intrathoracic pressure relations due to overdistension of the pulmonary cyst, and (2) symptoms of pulmonary suppurative disease following the development of infection of the cyst.

In spite of the recognition of the pitfalls in diagnosis as reported by various authors<sup>1-4</sup> the differentiation from a number of intrathoracic lesions frequently presents a difficult problem. The importance of establishing a correct diagnosis before operation will be brought out strikingly in the cases to be presented. Many of these demonstrate long morbidity and incapacitation or hospitalization for treatment of a condition other than the one to be discussed.

The present study is based on experience with thirty patients, twenty-seven of which had symptoms following the development of infection of the malformed area. In the remaining three, symptoms were produced when intrathoracic pressures became markedly disturbed through overdistension of the cyst. The age of the patients range from a few days to twenty-five years with the exception of one patient who was thirty-eight and another who was fifty-nine years. The lesions were fairly evenly distributed among the various lung lobes. In no case was there bilateral involvement. In a review of twenty-six reported cases by nine authors, the age distribution, duration of symptoms and location of lesions were approximately the same as in the present series.<sup>5-13</sup>

*Pathology* The gross pathologic picture in the thirty cases studied was classified as follows: (1) those which presented multiple cysts and considerable functioning lung, (2) those with

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\*From the Department of Surgery of the University of Chicago

multiple cysts but with little or no normally developed lungs, (3) those which presented a large amount of abnormally developed bronchial tree elements, a number of smaller cysts and little or no normally developed terminal respiratory units. This is an arbitrary classification based on the degree and character of involvement. The records of patients presented illustrate that at times this factor had considerable influence on the clinical course as well as the overall pathologic picture.

Microscopically viewed, the cysts were lined by columnar ciliated epithelium except when as a result of metaplasia it had been replaced by squamous epithelium or had been entirely destroyed by infection. The cysts were surrounded by a variable amount of fibrous connective tissue with bronchial wall elements such as cartilage, glands, and smooth muscle being present in some regions. Outside of the cystic areas many small air passages lined by cuboidal or low columnar epithelium were present. The amount of this type of abnormal development varied considerably in the sections of different patients. When infection had been present throughout the lung, the usual changes characteristic of pneumonitis, such as round cell infiltration, macrophages, and plasma cells, were present. The influence of diffuse chronic pneumonitis on the clinical picture as well as the diagnostic problem will be discussed in more detail under that heading.

The diagnosis of congenital cystic disease of the lung is usually not difficult when its possibility is kept in mind. In those cases where symptoms are produced by overdistension of the cyst with air, the conditions most frequently confused are spontaneous pneumothorax and diaphragmatic hernia. When fluid is present, empyema is suspected. When the patient is seen following the development of infection, lung abscess, bronchiectasis, tuberculosis, pneumonitis and chronic bronchitis are frequently diagnosed before the true nature of the lesion is discovered. In the present study the following conditions were diagnosed previous to recognition of the lesions: (a) bronchiectasis, 17, (b) lung abscess, 10, (c) empyema, 5, (d) tuberculosis, 5, (e) pneumothorax, 3, (f) pneumonitis, 3, (g) diaphragmatic hernia, 3, (h) chronic bronchitis, 1. In the 26 reported cases, a similar group of conditions was considered in differential diagnosis. In spite of the various diagnostic methods for studying these lesions, it is frequently extremely difficult to differentiate between one of the above lesions and that of cystic malformation of the lung. A careful history of the onset of the clinical course together with x-ray films of the chest and information from bronchoscopic examination will usually lead to a correct diagnosis in a high percentage of cases when the possibility of the lesion is kept in mind. The

following case reports are representative of difficulties encountered in making a diagnosis

*Lung Abscess* 1) An 18-year-old white male complained of having had pneumonia at the age of five years. Following this, a lung abscess developed and was drained through the chest wall. After a period of time the drain was removed. The symptoms of productive cough and sepsis returned, however. The abscess cavity was again drained and allowed to close on three successive occasions. The last drainage tube had been in place for approximately twelve years when the patient was first seen in this clinic. During this period he had developed normally and had no complaints other than the presence of the draining sinus.

Physical examination revealed a healthy appearing obese boy with a large tube draining a sinus at the base of the right lung posteriorly. On removing the tube, a smooth lined cavity approximately two to two and one-half inches in diameter was visible. Several bronchial fistulae were demonstrable. X-ray films following injection of the sinus with iodized oil showed a fluid level just below the dome of the diaphragm. The diagnosis of congenital cystic malformation of the lung was made and the right lower lobe was resected. The postoperative course was uneventful.

The surgical specimen showed a large cyst involving approximately one-third of the lower lobe, the remainder of the lobe being largely airless. A microscopic section through the larger portion of the lobe showed much of the lung abnormally developed. The cyst was lined with columnar ciliated or stratified squamous epithelium.

2) A 38-year-old white female was admitted to the clinic complaining of a productive cough with foul sputum of approximately one year's duration. Four weeks prior to the onset of her symptoms a tonsillectomy had been made. She had been treated with penicillin and streptomycin which gave temporary relief and at one time a thoracentesis was said to yield frank pus. She had lost thirty pounds in weight.

TABLE 1 CONGENITAL CYSTIC MALFORMATION OF THE LUNG  
DIFFERENTIAL DIAGNOSIS

	Authors	Reported
1 Bronchiectasis	17	4
2 Lung Abscess	10	2
3 Empyema	5	4
4 Tuberculosis	5	2
5 Pneumothorax	3	1
6 Pneumonitis	3	0
7 Diaphragmatic Hernia	3	0
8 Chronic Bronchitis	1	0
9 Pleuropericardial cyst	0	1
10 No diagnosis	0	11
No Cases in Each Series	30	26

On admission she appeared chronically ill, had a fever of 38° C and a leukocytosis of 16,700. The hemoglobin was 11.5 grams and the red count 3.7 million. The positive physical findings were limited to the right chest which showed some decrease in tactile fremitus and a few moist rales in the mid-lung field posteriorly. The sputum raised by the patient was extremely foul, quite thick and greenish-yellow in color. It contained a variety of organisms commonly found in pulmonary suppurative lesions. There were no acid-fast organisms although the patient had been suspected of having had tuberculosis and was kept in a sanatorium for approximately two weeks. An x-ray examination revealed a fluid level containing cavity with a relatively small amount of infiltration surrounding, located in the right mid-lung field posteriorly. The diagnosis was nontuberculous lung abscess. Bronchoscopic examination showed much foul thick pus coming from the right lower lobe.

The patient was prepared for operation by chemotherapy and blood transfusions and the right lower lobe was removed. The upper lobe appeared normal. Her convalescence was entirely uneventful. The surgical specimen when opened showed a large cavity in the upper part of the right lung posteriorly. A moderate amount of fibrosis was present about the cavity. The lower portion of the lung appeared normal. A microscopic section made through the entire wall of the cavity revealed an abnormally developed lung with the cavity lined by columnar ciliated epithelium except in some places where it had been replaced by squamous epithelium.

The diagnosis of lung abscess in this patient was a very natural one in view of the onset of a productive cough a short time following tonsillectomy, since that operation under anesthesia is one of the more frequent causes of lung abscess. When the lesion did not decrease in size under medical management, in spite of the clinical picture being markedly improved, a suspicion of malformation of the lung should have been entertained. This was especially true when the patient was first seen in this clinic a year following the onset of her illness. A large pulmonary cavity presenting a fluid level, unaccompanied by sepsis or a positive sputum for tubercle bacilli, is most likely to be a congenital lung cyst.

In patients having chronic pneumonitis surrounding cystic areas, the diagnosis of lung abscess is a common error. In such cases after drainage of the cavity the space does not become obliterated. If a biopsy is not taken, the true nature of the disease may remain unrecognized and a number of operations may be made in trying to heal the lesion. In such cases the history should arouse one's suspicion of the possibility of the condition. When the correct diagnosis is made, operative treatment should consist of excision rather than drainage unless contraindicated by the patient's general condition. Next to bronchiectasis, lung abscess has been diagnosed most frequently in the present series of cases prior to recognition of the true nature of the lesion.

*Bronchiectasis* P K, a white female 25 years of age, complained of a productive cough with intermittent attacks of fever over a period of twenty-four years. She had had whooping cough at the age of one year and had developed pneumonia during her second pregnancy. Examination revealed a poorly nourished, chronically ill individual who coughed considerably during the procedure. Many rales were heard in both bases. X-rays following iodized oil injection showed the characteristic picture of bilateral bronchiectasis. On bronchoscopy a purulent exudate was seen coming from the bronchus of all lobes. A diagnosis of bilateral bronchiectasis was made and the patient was prepared for operation. A resection of the right lower and middle lobes was carried out by the dissection technic. Her postoperative course was uneventful. Her symptoms were decreased to approximately one-third of the original severity and her general condition was good. Examination of the surgical specimen showed the lesion in the lower lobe to be saccular bronchiectasis. However, the right middle lobe was found to be made up entirely of cystic areas. Microscopic sections of this lobe showed the characteristic picture of cystic malformation of the lung. Approximately seven months following the above operation the left lower lobe and lingula were resected. The patient made a good recovery and has been largely relieved of her symptoms.

This patient presented the usual history and findings of bilateral bronchiectasis, the true nature of the lesion in the middle lobe being found only after the surgical specimen was examined. One might speculate as to whether infection of the cyst in the middle lobe had led to the development of bronchiectasis in the lower lobes due to repeated contamination by internal drainage.

In three other patients of the group under study, the middle lobe was involved by the malformation. In these cases there was no infection in the lower lobes and on iodized oil injection pathological changes were seen only in the middle lobe. From our experience with the present group of cases it would seem that when only the middle lobe is involved by a suppurative process, cystic malformation should be suspected rather than primary bronchiectasis. In patients with middle lobe involvement, internal drainage of secretions into the lower lobes may produce a picture on bronchography suggestive of tubular bronchiectasis and thus lead to the resection of normal lung tissue. At times it may also suggest that the bilateral involvement is too severe for operation to be advisable. In the three above mentioned patients, the middle lobe was resected followed by complete relief of symptoms.

*Chronic (Diffuse) Pneumonitis* 1) An eight-year-old white male was first seen complaining of a productive cough with intermittent hemoptysis and fever of approximately one year's duration. The patient gave a history of bilateral pneumonia with surgical drainage of bilateral empyema during the earlier part of this period. On examination he appeared chronically ill and was somewhat dyspneic. The entire left lung was dull to flat, and breath sounds were either absent or bronchial.

in character. The right lung was normal. Laboratory findings included hemoglobin, 10 gms., red blood count, 3.9 million, and white blood count, 14,000. X-ray films showed the left lung to be entirely airless with a slight deviation of the heart shadow toward the right side. Following the injection of iodized oil, only the primary bronchi of the upper and lower lobes were outlined. On bronchoscopic examination a moderate amount of foul pus exuded from the left main stem bronchus and an especially large amount from the left lobe. The right side was clear. The differential diagnosis included massive empyema, chronic suppurative pneumonitis with abscess formation, and possibly bronchiectasis. Pneumonitis, however, was thought to be the most likely cause of his trouble. A thoracentesis revealed no evidence of pus in the pleural cavity. Therefore, after preparation of the patient for operation by several transfusions aggregating a total of 900 cc of whole blood and postural and bronchoscopic drainage as well as chemotherapy, an exploration was made. The left upper lobe was found to be completely atelectatic but not infiltrated or otherwise abnormal. The left lower lobe was diffusely infiltrated and airless, but no large cystic spaces could be identified. The lower lobe was removed by the dissection technic, and although the upper lobe could not be re-expanded, it was not resected.

Following operation the patient made an uneventful recovery. The upper lobe remained completely atelectatic for a period of approximately four to six weeks then became inflated spontaneously.

On cut section the surgical specimen revealed several cavities filled with frank pus. The remainder of the tissue consisted of markedly fibrosed and consolidated lung. On microscopic examination the walls of the spaces were lined by columnar ciliated or stratified squamous epithelium, and various elements of the bronchial wall were present. The remainder of the lung showed abnormal development of the various lung elements, numerous small spaces lined by cuboidal epithelium and much fibrosis. There was a complete lack of normally developed terminal respiratory units. The degree of infection was not as great as suspected from gross examination of the tissue.

2) A 10½-year-old female entered the hospital with a diagnosis of chronic lung abscess of two years duration. Two weeks prior to her pulmonary symptoms, her tonsils had been removed under general anesthesia. Following this she began to have a productive cough of green purulent sputum, associated with fever and other symptoms of sepsis. After treatment by conservative methods for one year, a cavity in the lower part of the right lung was drained with a tube. The patient has continued to drain from this area since and on several occasions there have been mild hemorrhages. She has lost eight pounds in weight and tires easily. There has been no exposure to tuberculosis.

Examination revealed a poorly nourished, chronically ill girl who was running a low grade fever. The leukocyte count was 8,900, hemoglobin, 11.3 grams and RBC, 3.7 million. Except for clubbing of the fingers, the positive physical findings were limited to the thorax where a rubber tube drain was seen in the 7th right interspace. Expansion of the right chest was markedly limited and tactile fremitus diminished. Breath sounds over the right chest were entirely absent and the percussion note was flat. X-ray films of the chest showed a diffuse opacity involving the entire right side with what appeared to be a cavity formation in the lower portion. The left lung was clear. The diagnosis was lung abscess.

with questionable empyema Bronchoscopic examination revealed some pus coming from the right main bronchus

The patient was prepared for operation by chemotherapy, supportive measures including blood transfusions On exploration the entire right lung was found to be infiltrated and airless Because the lesion involved the entire lung it was thought best to do a pneumonectomy For the first two weeks after operation the patient had an uneventful convalescence, but evidence of empyema developed at that time This was drained and subsequently a thoracoplasty was performed to obliterate the space The patient has remained asymptomatic since

On opening the surgical specimen one large, multi-loculated cavity was found involving a large portion of the lung The remainder of the lung was airless, infiltrated and fibrotic A microscopic section made through the entire lesion revealed the lining of the cavity to be columnar ciliated epithelium except where it had been replaced by squamous epithelium Outside of the main cavity other evidence of malformation of the lung was present

In patients with a pathological process such as the above described, it is frequently impossible to differentiate between a chronic pneumonitis and other pathologic lesions A history of insidious onset of a pulmonary suppurative process in a child without the usual etiologic factor for the production of bronchiectasis or lung abscess should strongly suggest the possibility of congenital cystic disease Bronchoscopic examination and x-rays following iodized oil injection are usually not diagnostic In such cases when the patient's condition warrants it and a thorough preparation for operation has been made, exploration and resection of the involved portion is indicated

*Empyema* A white female, 2½ years of age, was admitted complaining of some difficulty in breathing and a productive cough of two months' duration She had also had some elevation of temperature during this period Examination revealed an underdeveloped and undernourished sickly child whose right chest was dull to flat over the lower three-fourths of the lung A few rales were heard at the apex Breath sounds were diminished or absent over the greater portion of the right side The white count was nineteen thousand X-ray films of the chest revealed complete opacity in the lower two-thirds of the right lung An empyema was then diagnosed and drainage was recommended At operation after resecting a piece of rib the cavity was entered However, the wall did not appear to be that of an inflamed pleura, thus, a biopsy was taken This showed the condition to be a large cyst of the right lower lobe lined by columnar ciliated epithelium After the cyst had drained for a period of approximately two years, resection of the right lower lobe was carried out without event

As pointed out by Maier and Haight<sup>1</sup> large infected cysts of the lung are commonly erroneously diagnosed as empyema In some cases x-rays following diagnostic pneumothorax may be helpful in differential diagnosis in that the limits of the cavity may appear to be more rounded than is usually the case in empyema Also at

operation the tissue outside of the cavity does not appear to be inflamed in that it is less rigid than is the case in the wall of an empyema. A routine biopsy of the wall is usually diagnostic. Since this diagnosis is usually made in infants or small children, drainage of the cyst prior to resection may frequently be the treatment of choice. However, a correct diagnosis is necessary for determining prognosis and the planning of further care. In most reported cases the diagnosis has been made following drainage of the lesion, and resection of the lung has been made at a later date.

*Pulmonary Tuberculosis* A 50-year-old colored male complained of a productive cough and fever of several years' duration. There was no history of night sweats or hemoptysis. On some occasions he had become dyspneic and had experienced pain in the left chest. Examination revealed a chronically ill-appearing individual who coughed considerably during the procedure. Many coarse rales were heard over the left chest, and bronchial breathing was marked in the lower half posteriorly. X-ray films showed marked opacity with cavity formation in the lower three-fourths of the left lung. Following iodized oil injection a large cavity was demonstrable in the lower left lung and a number of smaller loculations in other parts of the same side. Examination of the sputum showed several organisms which appeared like tubercle bacilli, and for a time pulmonary tuberculosis was diagnosed. Subsequent examinations of the sputum were negative for tubercle bacilli, however, and drainage of the lower cavity was planned. The patient's condition improved, and the operation was postponed. Because of the patient's age and general disability, resection of the involved lung was thought inadvisable. He has been seen at infrequent intervals during the past nine years and has continued to have a negative sputum for acid fast organisms and has a moderately productive cough but without causing undue handicap. The final diagnosis was congenital cystic malformation of the left lung.

Five of the present series of cases and two of the reported cases had been treated for pulmonary tuberculosis before the true nature of the lesion was recognized. When the possibility of cystic malformation is kept in mind, however, this error in diagnosis is much less likely. Three of the patients had been seen a number of years ago before congenital cystic malformation of the lung was well known. In patients having a productive cough with x-ray evidence of a cavity presenting a fluid level, a repeatedly negative sputum for tubercle bacilli should rule out the diagnosis of pulmonary tuberculosis.

*Spontaneous Pneumothorax* A 3-year-old colored female was admitted complaining of a mild productive cough, fever and dyspnea of one month's duration. Shortness of breath had not been extreme at any time, and the amount of sputum raised was rather small. Examination revealed a normally developed child of three who did not appear ill. Positive findings were limited to the chest. Rales were heard in both lungs and there was dullness in the lower part of the right side. Breath



sounds were diminished or absent over the upper two-thirds of the right lung. On x-ray examination the right lung appeared to be almost completely collapsed by a spherical shaped space filled with air. The mediastinum was not shifted. The diagnosis was spontaneous pneumothorax. Further examination revealed no evidence of other lesions, and the tuberculin test was normal. Manometric readings showed approximately atmospheric pressures within the air space, the pressure decreasing on inspiration and increasing on expiration. After removing several hundred cubic centimeters of air from the space, the pressures were unchanged. Fluoroscopic examination showed the space to be the same size as before the aspiration.

On closer inspection of the x-ray films it was seen that the outline of the air-filled space was oval in shape. Both at the apex and at the base there was a continuous border encircling this ovoid space. This suggested that the space was within the lung with a very thin shell of lung surrounding it. Therefore, a diagnosis of congenital cystic malformation of the right lung was made.

The patient has been seen at infrequent intervals during the subsequent ten years, and her condition has remained essentially the same. Operative removal of the cyst has been advised and rejected.

Pressure symptoms produced by large cysts of the lung usually occur in young children or infants. In former years a number of these cases have probably been diagnosed as spontaneous pneumothorax, and when complete examinations were not made the true nature of the condition went unrecognized. Four of the present series studied, whose symptoms were produced by intrathoracic pressure changes, were three years of age or less, one being only twelve days old. The x-ray appearance of a spherical outline is highly suggestive of the presence of a large cyst, but is not always conclusive. If the condition persists unchanged for a long period of time, cystic malformation of the lung is the most probable diagnosis. This can usually be determined by establishing a pneumothorax, thus demonstrating the cyst wall, or by the injection of an opaque media such as iodized oil into the cystic space and visualizing the outline of the cyst wall and trabeculae on x-ray examination.

*Chronic Bronchitis* A 16-year-old white female was first seen complaining of repeated attacks of an upper respiratory infection which produced a chronic cough. This had not kept her from attending school and had not impaired her general health to any considerable degree. Physical examination revealed a well-developed and nourished individual who did not appear to be very ill. The general physical examination as well as that of the chest was entirely normal. Fluoroscopy showed no abnormal findings. A diagnosis of chronic bronchitis was made, and the patient was treated with sulfa drugs and cough medicine. She was seen at infrequent intervals and continued about the same with intermittent exacerbations of her upper respiratory infection. Approximately one year later during a recurrence of her symptoms, an x-ray picture was made which showed two or three spherical cavities demonstrating

a fluid level and located in the lower right lung field. On physical examination a few rales were heard in the right base. The diagnosis was congenital cystic malformation of the right lung. At operation the condition was found to be confined to the right lower lobe which was removed by the dissection technic. The patient made an uneventful recovery and has been asymptomatic during the two year interval since operation.

The surgical specimen contained two large and several small multi-loculated cystic spaces which were almost completely surrounded by normally developed and inflated pulmonary tissue. Microscopic examination revealed columnar ciliated and stratified squamous epithelium lining the cystic spaces. A considerable amount of fibrous tissue and some abnormally developed respiratory passages were present in the walls of the cyst. However, approximately one-half to two-thirds of the lung parenchyma appeared to be normally developed.

The above case illustrates that cystic areas may be easily overlooked both on physical and fluoroscopic examination when little or no secretion is present and where normally functioning lung tissue surrounds the cyst. Furthermore, when the cysts are located below the level of the dome of the diaphragm posteriorly, they are not demonstrable on antero-posterior x-ray views of the chest. A mild cough with little sputum may be the only symptoms present. The condition may go unrecognized until infection increases the fluid contents of the cysts. A history of continued cough in children or young adults without obvious cause should be looked upon with suspicion and repeated fluoroscopic and x-ray examination made for evidence of the lesion.

Treatment consists of resection of the involved part. The risk of operation is small when the patient is properly prepared. In the present group of thirty patients there was one pneumonectomy, one bilateral resection, two bilobectomies. The remainder had one lobe removed. Complete relief of symptoms followed removal of the diseased part. There were no deaths.

It has thus been shown that many conditions of the chest may be clinically simulated by cystic malformation of the lung. In addition to those illustrated by case presentation, bronchogenic carcinoma located in the periphery of the lung may sometimes be confused with this condition. A fluid containing cyst may present a circumscribed opacity on x-ray examination not dissimilar to that produced by carcinoma. Both the cyst and the carcinoma may for several months remain asymptomatic and be discovered only on routine fluoroscopic or radiographic examination. The differential diagnosis is usually made on the basis of the age of the patient and the x-ray appearance of the lesion. If the patient is under 30 years of age, the lesion is most likely to be a cyst of the lung. On x-ray examination a bronchogenic carcinoma is more apt to have less sharply defined borders and be less spherical.

shaped than a cyst. In some cases a definite diagnosis cannot be established without exploration. This is indicated in either case because resection of the lesion is indicated in both.

Three patients in this study were seen in consultation with Dr. M. M. Shaw and Dr. Ed Bryant and were treated at the Provident Hospital.

### SUMMARY

A review of thirty cases of cystic malformation of the lung revealed that a number of pathologic conditions had been diagnosed before the true nature of the lesion was recognized. In several instances treatment had been instituted for one or more of these lesions for periods of over a year. In twenty-six collected cases reported by nine authors, a similar experience was noted. The difficulties in differential diagnosis were based chiefly on the similarity of the clinical course with that of other pathologic conditions of the chest. Although radiographic and fluoroscopic examination remain the best diagnostic methods for differentiation, they are not infallible and must be correlated with the clinical findings. The pathologic diagnosis is important both for an accurate evaluation of the disease and for proper surgical treatment. Since the risk of operation is small, resection of the involved lung is the treatment of choice.

### RESUMEN

Un repaso de treinta casos de anomalías quísticas del pulmón reveló que se habían diagnosticado varios otros estados patológicos antes de que se reconociera la verdadera naturaleza de la lesión. En algunos casos se habían instituido tratamientos para una u otra de estas lesiones por períodos de más de un año. En veinte y seis casos compilados, sobre los cuales informaron nueve autores, se notaron experiencias semejantes. Las dificultades encontradas en el diagnóstico diferencial se debieron principalmente a la semejanza del curso clínico al de otros estados patológicos del tórax. Aunque el examen radiográfico y radioscópico todavía es el mejor método para el diagnóstico diferencial, no es infalible y debe ser correlacionado con los hallazgos clínicos. El diagnóstico patológico es importante tanto para apreciar la enfermedad correctamente como para escoger el tratamiento quirúrgico apropiado. Ya que la operación acarrea poco riesgo, la resección del pulmón afectado es el tratamiento de elección.

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# Pulmonary Embolism. A Precipitating Factor of Acute Coronary Insufficiency\*

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Cardiac involvement following pulmonary embolism has been so commonly attributed to acute cor pulmonale that the fact that the left ventricle may be affected as often as the right ventricle has been overlooked. It should be recognized that not only does coronary insufficiency frequently develop following acute massive pulmonary embolism but that it may be the predominant cause of the cardiac sequelae, morbidity and mortality.

Acute coronary insufficiency results from disproportion between the nutritional requirements of the myocardium and the coronary blood flow. In previous publications<sup>1,2</sup> we have presented the concept of acute coronary insufficiency as a complete clinical entity with distinct etiology, pathological physiology, characteristic anatomic, electrocardiographic and clinical features, and treatment. Acute coronary insufficiency may be the result of relative insufficiency of coronary flow due to increased cardiac work, or of absolute diminution of coronary flow, or of anoxemia occurring with a normal coronary flow. In most cases, a combination of these factors prevails and if the ensuing myocardial ischemia and anoxia are sufficiently severe or protracted, infarction or necrosis of the myocardium may develop. Myocardial necrosis may be either gross or microscopic. It is generally focal and disseminated, rather than massive and circumscribed, as in acute coronary occlusion. Characteristically, necrosis is localized in the subendocardial layer and the papillary muscles, the areas most susceptible to ischemia and anoxia. The endocardium and the pericardium usually are not affected.

The electrocardiogram of acute coronary insufficiency without acute occlusion is distinguished from the electrocardiogram of acute coronary occlusion by depression of the RS-T segment and inversion of the T-wave in one or more leads, without RS-T elevation or deep Q-waves. The changes, which often appear in all the standard and precordial leads, are generally reversible and

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transient, in contrast to the changes of acute coronary occlusion which are of long duration or permanent. The depression of the RS-T segment has been attributed to the subendocardial localization of the myocardial ischemia.<sup>2</sup>

Since the report of McGinn and White,<sup>3</sup> in 1935, on the electrocardiogram in pulmonary embolism, many authors have drawn attention to the so-called acute cor pulmonale pattern. This pattern is characterized by a deep S-1 and Q-3, depression of the RS-T interval in lead I and elevation of the RS-T interval in lead III, and inversion of T-3 or both T-2 and T-3. These changes have been attributed to acute right ventricular dilatation or strain resulting from the obstruction of the pulmonary artery. In our experience, as well as in that of other investigators,<sup>4,5,6</sup> this electrocardiographic pattern occurs in only a minority of cases of pulmonary embolism. In the majority of cases the electrocardiographic changes are less characteristic, consisting chiefly of RS-T depressions and T-wave inversions in one or more leads, without a deep S-1 or Q-3. Right ventricular strain cannot be considered the sole underlying cause of changes of this type since similar changes have been observed following acute coronary insufficiency precipitated by such causes as shock and hemorrhage.<sup>2</sup>

Horn, Dack and Friedberg<sup>7</sup> pointed out that acute coronary insufficiency following pulmonary embolism not infrequently resulted in ischemic changes in the left ventricular myocardium. These authors found either gross or microscopic infarction of the left ventricle, in the absence of acute coronary occlusion, in approximately one-fifth of 42 fatal cases which they examined. They believe that myocardial infarction was due to acute coronary insufficiency resulting from anoxemia and shock. Similar pathological observations were recently reported by Currens and Barnes,<sup>8</sup> who attributed the myocardial ischemia and infarction to increased right ventricular pressure and diminished coronary blood flow.

### *Material and Results*

This report is based upon a clinical and pathological study of forty fatal cases of massive pulmonary embolism (confirmed at autopsy) in which electrocardiograms were recorded following the embolism.

The electrocardiograms were classified in three groups. Group I consisted of 14 cases presenting the electrocardiographic pattern of acute cor pulmonale (Fig 1). Group II consisted of 17 cases in which the electrocardiograms showed the changes of acute coronary insufficiency, namely, depression of the RS-T interval in two or more leads with or without inverted T-waves (Fig 2).

Deep S or Q waves and distinct RS-T elevation were absent. In group III were placed nine cases of which 6 showed atypical QRS and T-wave changes, and 3 failed to show any recent changes. In the latter cases the electrocardiograms prior to the pulmonary embolism were very abnormal.

Atypical right bundle-branch block was observed in 3 cases of the cor pulmonale group (Group I). The conduction defect persisted until death in all 3 cases. In addition, various disturbances in cardiac rhythm were observed, nodal rhythm in 2 cases, supraventricular tachycardia in 2 cases, auricular fibrillation in 1 case, sino-auricular block in 1 case, and A-V block in 1 case.

A comparison was made of the influence of various predisposing and precipitating factors of coronary insufficiency in Groups I and II. These included age, antecedent cardiac or coronary disease, cardiac enlargement, right ventricular strain, and anatomic changes observed in the myocardium at autopsy. Electrocardiographic changes attributable to acute coronary insufficiency were

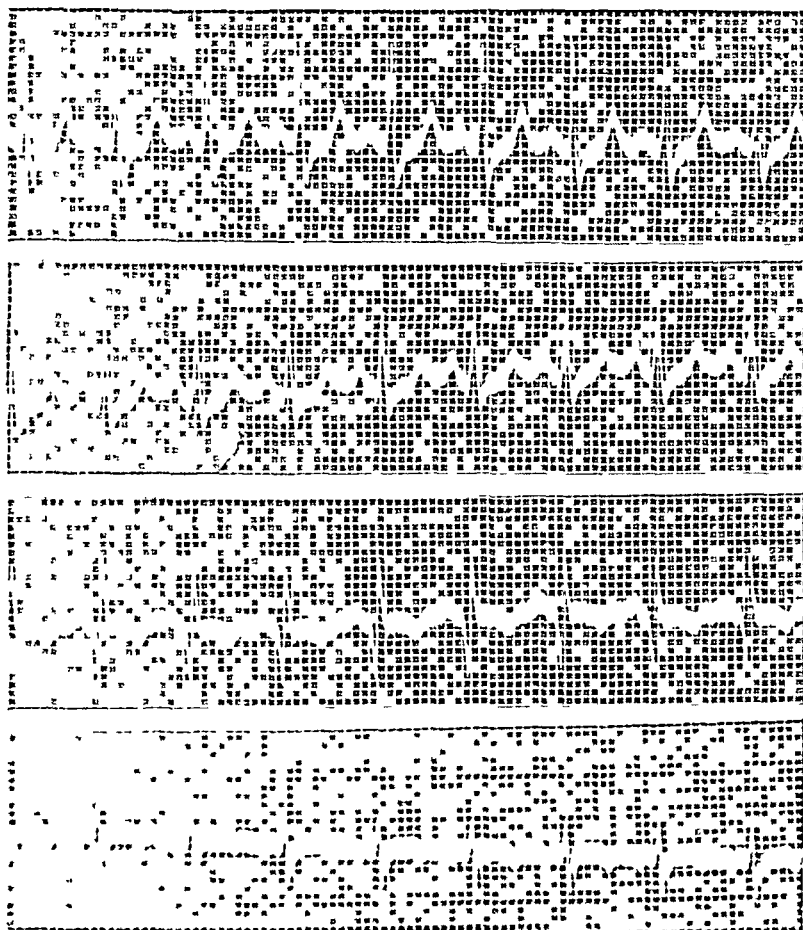


FIGURE 1

found for the most part in the older individuals and in those with clinical or anatomical evidence of antecedent coronary sclerosis and cardiac enlargement, more particularly in those whose previous electrocardiograms were very abnormal (Fig 3) In other words, acute coronary insufficiency is more likely to follow pulmonary embolism in patients who are suffering from chronic coronary insufficiency than in individuals who have previously been free of cardiac abnormalities On the other hand, the classical *cor pulmonale* pattern occurred most often in patients whose hearts were previously normal in size and free of coronary sclerosis

Acute dilatation of the right ventricle without significant dilatation of the left ventricle was noted postmortem in almost one-half of the cases (45 per cent) In at least one-half of these cases the electrocardiographic changes were indicative of acute coronary insufficiency, the changes associated with acute *cor pulmonale* were not present

Detailed anatomic study of the myocardium and the coronary arteries revealed acute myocardial necrosis or focal myocardial infarction of the left ventricle, in the absence of acute coronary occlusion, in 9 cases The myocardial infarction was generally focal, disseminated, located in the subendocardial layer, in a number of instances it was localized in the papillary muscles of the left ventricle Gross changes were visible in 3 cases (Fig 4) and microscopic changes in 6 cases These changes were like those found in postmortem examination of cases of acute coronary

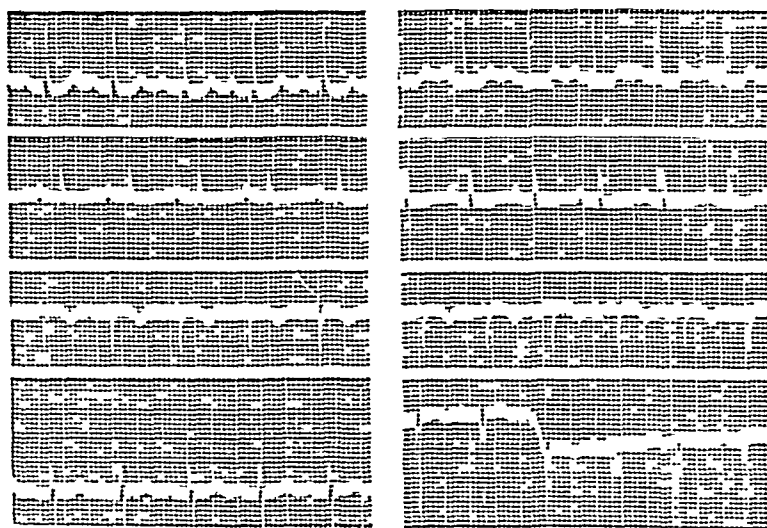


FIGURE 2



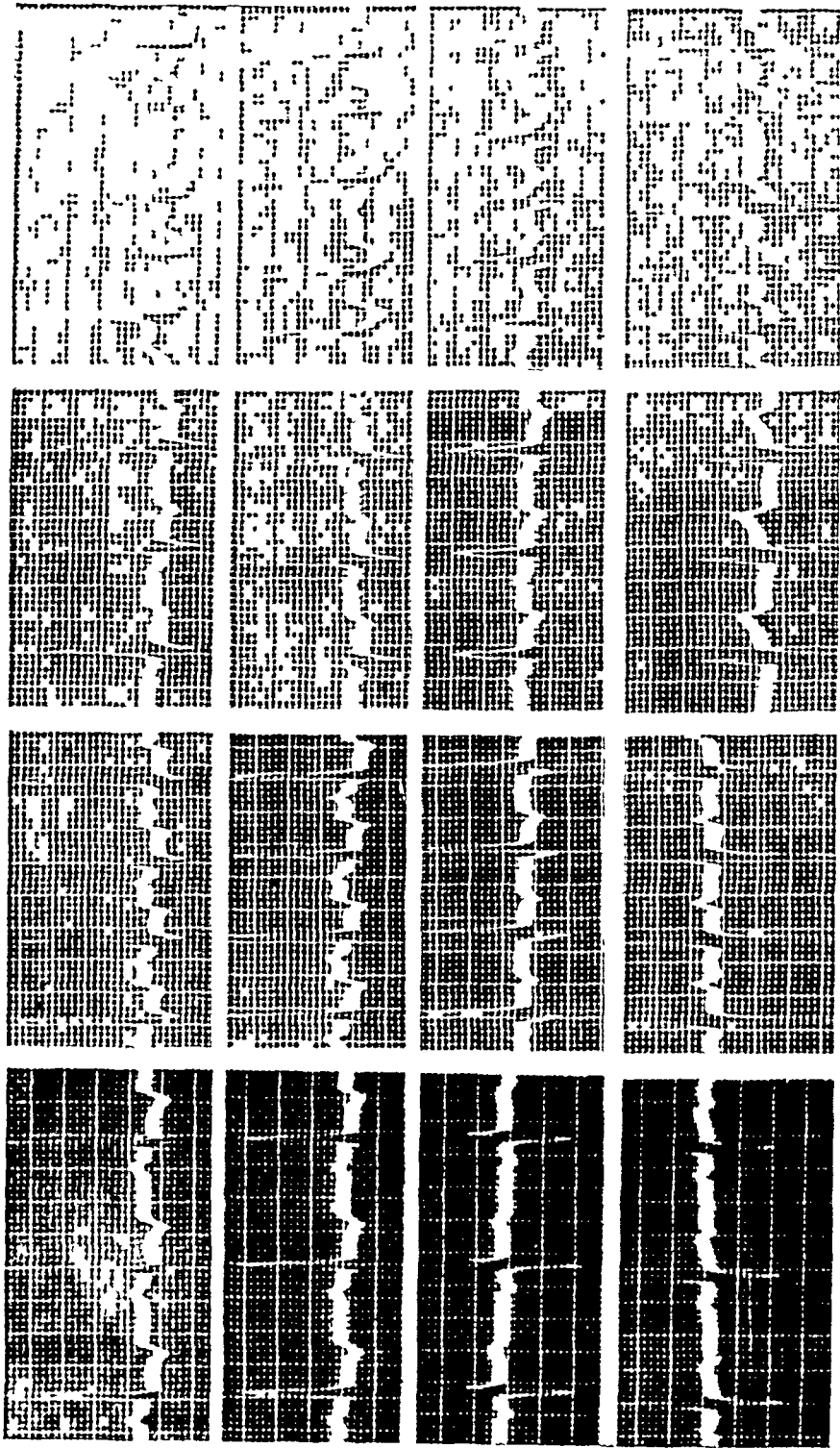


FIGURE 3

insufficiency precipitated by such factors as hemorrhage and shock<sup>2</sup> In all nine cases, the left ventricle was involved, the anterior and posterior walls with equal frequency Infarction of the right ventricle occurred in one case

One of the nine cases with myocardial necrosis was in Group III, four were in Group I and four in Group II Ischemic changes in the myocardium, then, occurred as often in patients with electrocardiographic signs of acute cor pulmonale as in those with acute coronary insufficiency However, the myocardial changes in the coronary insufficiency group were more extensive and more severe than the changes that occurred in the cor pulmonale group Gross myocardial infarction was observed only in the coronary insufficiency group (Group II)

Antecedent arteriosclerotic or hypertensive heart disease was present in all 9 cases of focal myocardial infarction In four instances the coronary arteries were distinctly narrowed In the remaining five cases, in which the coronary arteries were normal or only minimally narrowed, another factor predisposing to coronary insufficiency, such as hypertension and cardiac hypertrophy, was present Five of the patients had sustained recurrent pulmonary emboli and had survived the initial episode for two to three weeks (Figs 2 and 3) The coronary insufficiency precipitated by the recurrent pulmonary emboli was, therefore, sufficiently prolonged for anatomical myocardial changes to develop<sup>7</sup> If death takes place soon after the occurrence of the embolism, myocardial infarction may not be demonstrable regardless of the severity of the myocardial ischemia

#### *Discussion*

Clinical and pathological analyses of 40 fatal cases of massive pulmonary embolism lead to the conclusion that acute coronary



FIGURE 4

insufficiency plays as large a part as does acute cor pulmonale in the cardiac sequelae of pulmonary embolism. In our series the electrocardiographic signs characteristic of acute coronary insufficiency appeared more frequently than the changes associated with acute cor pulmonale. Moreover, coronary insufficiency not infrequently resulted in myocardial necrosis or infarction of the left ventricle.

Acute coronary insufficiency following pulmonary embolism may be caused by anoxemia, shock, right ventricular strain, and possibly reflex coronary vasoconstriction. Anoxemia, a marked clinical feature of pulmonary embolism, is manifested by dyspnea, tachypnea, and cyanosis. It is the result of diminished blood flow through the lungs and diminished arterial oxygen saturation. In spite of the fact that in experimental investigation<sup>9 10</sup> it has been found that a large cross section of the pulmonary artery must be mechanically obstructed before significant interference with the pulmonary circulation develops, it is well known that in human beings relatively small emboli may produce distinct pulmonary hypertension and circulatory effects. These effects have been attributed to widespread reflex vasoconstriction of the pulmonary arterioles mediated through the vagal nerve endings.<sup>11</sup> That profound vagal stimulation may occur was made manifest by the disturbances in cardiac rhythm that appeared in some of our patients and in animals following experimental pulmonary embolism.

Anoxemia and asphyxia may produce electrocardiographic changes indistinguishable from those produced by acute coronary insufficiency.<sup>12 13</sup> The underlying cause of the changes is anoxia of the myocardium, which, if intense or associated with insufficient coronary blood flow, may result in myocardial necrosis of the left and right ventricles.

Coronary insufficiency may be precipitated by shock, with its associated diminution of circulating blood volume, diminished cardiac output, diminished venous return to the heart and lowering of arterial blood pressure. Recent experiments<sup>11 14 15</sup> show that pulmonary embolism and increased pressure in the pulmonary artery are accompanied by immediate drop in systemic blood pressure and cardiac output. This drop was attributed to obstruction of venous return from the lungs to the heart<sup>15</sup> and to a reflex depressor mechanism between the lungs and the heart.<sup>11 16 17</sup> The hemodynamic effects of the shock and lowered systemic blood pressure will result in diminution of coronary blood flow.

When the coronary circulation is impaired by antecedent coronary sclerosis or cardiac hypertrophy and the myocardial ischemia secondary to the diminished coronary blood flow is severe or

prolonged, necrosis and infarction of the myocardium take place. The site of necrosis may be the left ventricle alone, or both the left and the right ventricles. Currens and Barnes<sup>6</sup> reported one case of isolated infarction of the right ventricle in pulmonary embolism, but this was not observed among our patients or in the series reported by Horn, Dack and Friedberg.<sup>7</sup> It may be concluded that the left ventricle is more susceptible than the right ventricle to the anoxic or ischemic effects of coronary insufficiency. The left ventricle is also the more susceptible in acute coronary occlusion, in which infarction of the right ventricle is rare except by direct extension from the left ventricle. The sites of predilection for focal infarction in the left ventricle in pulmonary embolism, as in other types of acute coronary insufficiency, are the subendocardial layer and the papillary muscles.

Reflex coronary vasoconstriction mediated through the vagus nerve<sup>16</sup> may be a factor in initiation of coronary insufficiency in pulmonary embolism. However, the validity of this reflex mechanism has been debated for many years, and recent experimental observations<sup>15-19</sup> support the opinion that this theory is ill founded. In any event, the hemodynamic effects of pulmonary embolism are so powerful that such a reflex mechanism need not be called into play.

Right ventricular dilatation and strain secondary to obstruction of the pulmonary artery is another agent responsible for precipitating coronary insufficiency in pulmonary embolism.<sup>11</sup> Right ventricular dilatation undoubtedly occurs,<sup>20</sup> since not infrequently it may be demonstrated during life,<sup>4</sup> and it was found at necropsy in almost one-half of the hearts in our series. However, it was not, in every instance, associated with electrocardiographic signs of cor pulmonale, in half of the cases in which isolated right ventricular dilatation was found postmortem, the electrocardiogram showed changes characteristic of acute coronary insufficiency. Furthermore, focal myocardial infarction of the left ventricle occurred as often in the presence of right ventricular strain as in its absence. It seems apparent that acute coronary insufficiency may be the predominant factor underlying electrocardiographic changes and myocardial involvement, even when right ventricular strain exists.

It has been observed experimentally<sup>21</sup> that increased right ventricular pressure may produce diminution in coronary blood flow, particularly in the right coronary artery, by increasing the resistance to blood flow within the coronary vessels. This may explain the resemblance of the classical pattern of acute cor pulmonale in the electrocardiogram to that of posterior wall infarction of the left ventricle, since the right coronary insufficiency may result

in greater ischemia of the posterior wall than the anterior. It may also result in greater ischemia of the right ventricle. Nevertheless, this is difficult to confirm postmortem, since the focal infarction is not localized to the posterior wall of the left ventricle but occurs with equal frequency anteriorly and posteriorly, and involves the right ventricle alone in only a small minority of cases.

### SUMMARY

A clinical and pathological study of 40 necropsied cases of massive pulmonary embolism indicates that acute coronary insufficiency plays as large a part as does *cor pulmonale* in the cardiac sequelae of embolism.

Electrocardiographic changes attributable to coronary insufficiency occurred more often than the classical *cor pulmonale* pattern. They were more common in older patients with antecedent coronary sclerosis and cardiac enlargement, whereas the classical *cor pulmonale* pattern occurred most often in patients with normal coronary arteries and heart size.

Focal subendocardial infarction of the left ventricle, in the absence of acute coronary occlusion, was found postmortem in nine cases. This resulted from coronary insufficiency precipitated by the pulmonary embolism, in patients with antecedent coronary disease and cardiac hypertrophy who had sustained recurrent emboli.

The various precipitating factors of coronary insufficiency following pulmonary embolism were evaluated. These were anoxemia, shock, right ventricular strain, and reflex coronary vasoconstriction. Of these, shock associated with diminished cardiac output and coronary blood flow was considered the most important.

It can be concluded that acute coronary insufficiency may be the predominant factor underlying the electrocardiographic changes and myocardial involvement in pulmonary embolism, even when right ventricular strain exists.

### RESUMEN

Un estudio clínico y patológico de 40 casos autopsiados de embolia pulmonar masiva indica que la insuficiencia coronaria aguda desempeña un papel tan importante como el *cor pulmonale* en las secuelas cardíacas de embolias.

Alteraciones electrocardiográficas atribuibles a la insuficiencia coronaria ocurrieron más a menudo que el patrón clásico del *cor pulmonale*. Esas alteraciones fueron mas comunes en pacientes de edad mas avanzada, con antecedentes de esclerosis coronaria e hipertrofia cardíaca, mientras que el patrón clásico del *cor pul-*

monale ocurrió mas frecuentemente en pacientes con normales arterias coronarias y corazon de tamaño normal

En el examen autopsico de nueve casos se encontraron infartos subendocardiacos focales del ventriculo izquierdo, sin oclusión coronaria aguda Se debieron estos infartos a insuficiencia coronaria precipitada por la embolia pulmonar en pacientes con enfermedad coronaria e hipertrofia cardiaca antecedentes, que habían sufrido embolias repetidas

Se avaluaron los varios factores que precipitan la insuficiencia cardiaca subsiguiente a la embolia pulmonar Estos factores fueron anoxemia, choque, tension del ventriculo derecho y vasoconstriccion coronaria refleja Se creyo que el más importante de esos factores fue el choque asociado con la disminucion de la cantidad de sangre que expela el corazon y disminucion de la circulacion coronaria

Se puede concluir que la insuficiencia coronaria aguda puede ser el factor predominante de las alteraciones electrocardiograficas y de la lesion miocardiaca en la embolia pulmonar, aun cuando existe tension del ventriculo derecho

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## D I S C U S S I O N

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Dr Master's and Dr Dack's paper gives further additional evidence to reports appearing in the literature that the left ventricle is involved following pulmonary infarction, particularly in patients who have preexisting disease of the coronary arteries. The factor precipitating acute coronary insufficiency is undoubtedly the fall in blood pressure associated with shock that accompanies embolism to the lung. Currens and Barnes in 1943 reported 4 cases of myocardial infarction following pulmonary embolism involving the left ventricle wherein no significant obstruction was found in the coronary arteries to account for the acute infarction and they suggested that probably shock contributed in a great measure to the decreased coronary blood flow. However they found only these 4 cases out of a series of 30 hearts examined.

In order to determine what our records at the Brooklyn Hospital showed regarding this problem, we examined the charts of 28 patients that succumbed to a pulmonary infarction. These records were not selected but taken in the order of their occurrence and represent patients from the various services of the hospital. Twenty of these individuals had preexisting heart disease. In 15, death was sudden and unexpected and due to massive embolization consequently no electrocardiographic records were available. Of these remaining 13, none showed the characteristic electrocardiographic changes described by McGuinn and White, whereas in 2 of the charts there was some evidence that the myocardial infarct followed pulmonary embolization.

A female, age 54 years, who had hypertension was admitted to the Brooklyn Hospital for a gastro intestinal survey because of a suspected neoplasm, as she complained of loss of weight and vague intestinal symptoms

On the 1st hospital day she was suddenly seized with pain in the chest, expectorated blood and went into shock with the development of signs of pulmonary edema. The leucocyte count was 20,400, 94 per cent polys and the electrocardiogram showed inversion of the T wave in leads I and IVF. Changes similar to these described in Dr. Master's paper. That she had a pulmonary infarction there is no doubt, and it is very likely that the electrocardiographic changes represented acute coronary insufficiency involving the anterior wall of the left ventricle. She died 3 days following the acute episode and no autopsy was obtained.

A male, age 60, with hypertensive cardiovascular disease was admitted to the hospital following an acute myocardial infarction involving the anterior wall of the left ventricle. The electrocardiogram showed elevated R-T segments in lead I-II, and absent R and inverted T in lead IVF.

On the 10th day after admission he began to develop embolic manifestation in the lungs and following one of these episodes he went into shock. The electrocardiogram showed the development of deep Q2 and Q3 and elevated RT segments in leads II and III. It is interesting to speculate whether the pulmonary emboli were a causative factor in the development of the fresh infarct on the posterior surface of the left ventricle. No necropsy could be obtained.

Dr. Dack's study has given added emphasis to the occurrence of acute coronary insufficiency following pulmonary embolism and should make us more alert to detect evidence of this mechanism in the future. His studies may help us in explaining the series of events that developed in this patient.

A watchman, age 52, a diabetic of 4 years, was admitted to the medical wards of the Brooklyn hospital. He had no symptoms referable to his heart until one month before admission he complained of attacks of dyspnoea following climbing 2 flights of stairs. The night he entered the hospital he developed a severe attack of shortness of breath unassociated with pain in the chest. In the emergency ward he showed signs of shock and pulmonary edema. His heart was very rapid and the sounds were distant. The following day an x-ray of the lungs was reported as showing a zone of homogenous density in the right lower lung field. The area was triangular in outline with its base toward the chest wall and was highly suggestive of a pulmonary infarction. The electrocardiogram showed slight depression of the RT segments in leads 1, 2 and 3 and CF5 and was interpreted as a digitalis effect. Consultation with his local physician revealed the fact that he had been on Digitalis for the past 2 weeks.

Electrocardiogram taken 5 days later showed inversion of the T waves in lead 1, CF2, CF3, CF4 and CF5. These later changes indicated the possibility of anterior wall infarction. The tracing was again repeated 2 weeks later and it then showed a trend back toward the normal. There was less inversion in lead I and CF2 position and less inversion in CF3, 4 and 5. The x-ray was repeated at this time, and very scant



residual change were noted in the lower right lung field corresponding to the area of previously noted triangular density

The series of events were a pulmonary infarction followed by electrocardiographic changes highly suggestive of acute coronary insufficiency

From the work of Dr Dack and from our own findings the electrocardiographic changes as described by McGuin and White following acute pulmonary infarction are not seen too frequently. However there is some evidence in our records to support Dr Dack's contentions that the mechanism of acute coronary insufficiency may be a factor determining some of the cardiac effects of acute pulmonary embolism.

I am sure we all enjoyed Dr Master's presentation and I am grateful to have had this opportunity of taking part in the discussion.

# The Diagnosis and Treatment of Acute Laryngotracheobronchitis\*

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Acute laryngotracheobronchitis is a descriptive pathologic term for a disease of varied bacterial etiology. Despite its varied etiology the symptom complex generally fits into a definite pattern because the symptoms are produced by inflammation or obstruction of one or more of the breathing passages.

In past times it was generally assumed, and correctly so, that a child or an infant suffering from inflammation of the air passages or obstruction to breathing due to infection had diphtheria. That possibility should not be forgotten. Acute laryngotracheobronchitis, however, has occurred more commonly than has laryngeal diphtheria in recent years. It has been shown to have resulted from infection by hemolytic streptococci, *Streptococcus viridans*, *Staphylococcus aureus*, various pneumococci, *Haemophilus influenzae* and possibly on occasions by a virus.

The syndrome is seen in infants and children of all ages, but is more often a dangerous disease in children aged less than four years because of the relatively small size of the breathing passages. It is a disease most to be feared in those aged less than one year.

## *Clinical Picture*

The symptoms at onset of the disease are usually the same as those of spasmodic croup: a harsh brassy cough, and inspiratory stridor. These symptoms are generally due to subglottic edema, sometimes to supraglottic edema. Unless the vocal cords are involved the voice is not hoarse. Whatever the involvement of the region of the vocal cords, the classic signs of laryngeal obstruction are present: retraction above the suprasternal notch and clavicles, and of the epigastrium. Retraction of the intercostal spaces with inspiration is also often noted.

These symptoms at first may or may not be associated with fever. The absence of fever may correctly suggest that one is dealing with a case of spasmodic croup. However, my colleagues and I have seen several children whose dyspnea after an afebrile

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onset rapidly became very severe and who required tracheotomy within twelve to twenty-four hours after the onset. When dyspnea appears and increases in severity, fever and evidence of toxicity usually appear. If effective treatment is not instituted promptly, death may take place.

### *Pathology*

As the name implies, acute laryngotracheobronchitis is an acute inflammatory process involving the larynx, the trachea and the bronchi. Often edema is the only pathologic change noted. Secretion soon appears, especially in the lower part of the trachea and in the bronchi, and causes considerable mechanical obstruction to breathing. The secretion may be thick, ropy, gummy and tenacious, and frequently causes bronchial obstruction and atelectasis (fig 1). Inflammation and edema of the subglottic region are responsible for most of the symptoms of laryngeal obstruction.



FIGURE 1 Purulent secretions obstructing a bronchus (hematoxylin and eosin x120)



FIGURE 2 Cross sections of bronchi showing obstruction with thick secretions

(fig 2) Multiple regions of atelectasis may be present The secretion may become so thick as to form a cast of the tracheobronchial tree

### *Treatment*

The treatment of acute laryngotracheobronchitis is based on an understanding of the etiology and pathogenesis of the disease Thick secretions must be thinned, an infectious agent combated and constant vigilance maintained for evidence of respiratory obstruction In few other situations is constant intelligent nursing care so important

Thick secretions are most readily thinned by thoroughly moistening the air which the patient breathes A steam tent or steam room is usually the most convenient and effective means for supplying moist air Two or three steam kettles are usually necessary to provide humidity The water should literally drip from the top of the tent or from the ceiling The more modern mechanical humidifiers provide moisture without at the same time making the room uncomfortably hot Their use is to be preferred to that of a steam tent or steam room

Oxygen should be well moistened if its use becomes necessary, since unmoistened oxygen exerts an undesirable drying effect on the secretion of the respiratory tract Mechanical vaporizers<sup>1 2</sup> may be used in conjunction with an oxygen tent Lacking one of these we recently have used two nebulizers instead Distilled water was used as the fluid and an oxygen tank as the source of nebulizing force In times past steam has been run into the oxygen tent by pipe or rubber hose This method is cumbersome and unsatisfactory and may be dangerous Moist cloths suspended in the partially filled ice compartment of an oxygen tent and moistened frequently provide sufficient moisture to maintain the humidity at 70 to 80 per cent This, however, is not as high a humidity as is best to maintain

It has been shown<sup>3</sup> that carbon dioxide is an effective agent for liquefying bronchial secretions A 25 to 4 per cent mixture of this gas with 20 per cent oxygen in a tent has been suggested for treating pneumonia My colleagues and I have not used it but we think it worth trying

We often employ sodium or potassium iodide as an additional aid in liquefying tracheobronchial secretion Five drops of a saturated solution of one of these salts may be given three times daily to a child of two years, and three drops to a child of one year Davison<sup>4</sup> feels that the use of medicines is unnecessary if the inspired air is properly moistened and that the medicine may make the patient nauseated We agree but we have seen children

who seemed to have been helped by the administration of one of the iodides. We have not tried to use any of the other so-called expectorant drugs.

It is essential that the patient's intake of fluid be maintained. If the patient cannot take fluids by mouth, they should be given by the intravenous or subcutaneous route. In infants at least 2 fluid ounces (60 cc) per pound (0.5 kg) per twenty-four hours should be given and in older children about 1 fluid ounce (30 cc) per pound (0.5 kg).

One or more small transfusions (100 to 150 cc) of blood may be necessary as a supportive measure and to aid in combating the infection. The administration of concentrated blood plasma or blood serum has been suggested for its dehydrating effect on the laryngeal edema. We have not had any favorable results from its use in the few instances in which it has been tried. Concentrated human serum albumin might be tried.

Food may be given according to the child's desires. It is generally not desired during the acute phase except in liquid form.

It is very important that throat cultures be made. A suction apparatus such as was described several years ago<sup>5</sup> to collect material for typing of pneumococci is useful in obtaining material from infants for bacteriologic study. If tracheotomy is done, cultures of the tracheal secretions should be made.

Appropriate chemotherapy or antibiotic therapy varies from case to case depending on the etiologic bacterial agent. Penicillin is readily available at the present time and is effective when used to combat infections due to most strains of streptococci, staphylococci and pneumococci. It should be administered every two to three hours intramuscularly or by continuous intravenous infusion. Suggested dosage would be 200,000 units (divided into eight doses) daily for a child two years of age. If penicillin in a beeswax-oil medium is employed it is wise to use 200,000 to 300,000 units daily.

We prefer the use of procaine penicillin if a long-acting penicillin is to be used.

Large oral doses of penicillin can be given. In such acutely ill infants as those having acute laryngotracheobronchitis, one generally cannot depend on the oral route to provide adequate blood levels of the antibiotic agent.

Only rare strains of *Hemophilus influenzae* are killed by the use of penicillin. In fact one of the early uses of penicillin was to incorporate it in mediums on which *Hemophilus influenzae* was to be grown in order to kill off the other organisms which often overgrew it. *Hemophilus influenzae* infections respond well to the use of streptomycin. A total of 0.8 to 1.0 gm daily, given intramuscularly in four to eight divided doses, is suggested. A daily

dose of 0.5 gm will suffice in an infant less than one year of age

The sulfonamide drugs still are valuable therapeutic aids. Hemophilus influenzae infections sometimes can be treated successfully with sulfadiazine, as more often can those due to streptococci, staphylococci and pneumococci. If sulfadiazine cannot be tolerated by mouth it may be given subcutaneously in the form of a 5 per cent solution of the sodium salt. The usual precautions regarding the use of the sulfonamide drugs must be observed.

Tracheotomy is indicated if the patient's dyspnea increases and if signs of laryngeal obstruction become more marked despite the use of moistening apparatus. Evidence of extreme restlessness, cyanosis and fatigue also is an indication for tracheotomy. In addition demonstration by auscultation that there is diminished entry of air into both lungs is further evidence that the patient's airway has been greatly reduced in caliber. Tracheotomy is preferred to intubation. Ideally it is done after a bronchoscopic examination and after crusts and secretions have been sucked out through the bronchoscope and while that instrument is still in place.

Great care must be used when performing a tracheotomy on an infant to see that the incision is made at a sufficient distance below the larynx so that the tracheotomy tube will not irritate the subglottal region. When this precaution is not observed undesirable subglottal scarring may result.

After tracheotomy the air entering the tracheotomy tube must be kept moist, this aids greatly in the prevention of crusts that tend to form in the trachea. The same measures for moistening the air may be used postoperatively as preoperatively. My colleagues and I have found, however, that the use of a nebulizer

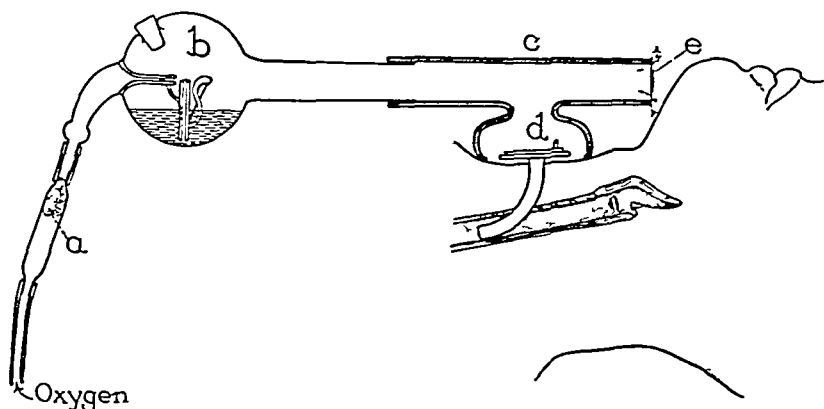


FIGURE 3 Nebulizer adapted to use for a tracheotomy tube (From Albers G. D. Use of a Nebulizer to Produce Oxygenated Vapor. Report of a Case of Acute Laryngotracheobronchitis. *Proc Staff Meet Mayo Clin* 18:511, Dec 29 1943)

as described by Albers<sup>6</sup> is most satisfactory (fig 3) A nebulizer is attached to a rubber tube that carries oxygen The distal end is applied to the tracheotomy opening by means of a flexible rubber hose Iams<sup>7</sup> reported that a small rubber nipple with the teat end cut off is satisfactory for this purpose In our experience this measure has been lifesaving Subsequent bronchoscopic aspiration is often unnecessary, the tracheal secretions can be aspirated by a catheter because they are kept moist Davison<sup>8</sup> urged that, when the suction catheter is used, it should not be inserted beyond the tracheotomy tube Occasionally it is necessary to aspirate more deeply When this is done very often the tracheal wall is irritated

### *Contraindicated Drugs*

It is still felt by some physicians that the struggling dyspneic infant having laryngotracheobronchitis should be given a sedative drug Such a practice is most unwise While the infant is under the influence of sedatives the cough reflex is often suppressed, secretions accumulate in the breathing passages and the infant dies from suffocation The sedative drugs obscure the signs and symptoms which might indicate a need for tracheotomy Infants having laryngotracheobronchitis rarely struggle unless some obstruction to breathing is present Therefore, the use of all opiates, barbiturates and other sedative or narcotic drugs is contraindicated

Likewise it is not wise to administer atropine or its related compounds to an infant having acute laryngotracheobronchitis Such drugs exert an undesirable drying effect on bronchial secretions

Occasionally asthma and laryngotracheobronchitis have been confused One might therefore be tempted to administer one of the so-called antihistaminic drugs Because of their possible sedative effect and atropine-like action, their use is contraindicated in the treatment of acute laryngotracheobronchitis

### SUMMARY

Acute laryngotracheobronchitis is a disease of varied bacterial origin It is a very serious disease but more so when it occurs in children less than one year of age Treatment consists in providing adequate moisture in the inspired air, sometimes the use of expectorant drugs, the administration of the proper chemotherapeutic or antibiotic agent, and careful nursing Tracheotomy is sometimes necessary Suggestions have been made regarding indications for its need, performance of the procedure and the after-treatment of the tracheotomized child Sedative and antihistaminic drugs are contraindicated in the treatment of acute laryngotracheobronchitis

## RESUMEN

La laringotraqueobronquitis aguda es una enfermedad de origen bacterico variado. Es una enfermedad muy grave, pero aun mas cuando ocurre en niños menores de un año de edad. El tratamiento consiste de humedecer adecuadamente el aire inspirado, del uso, a veces, de drogas expectorantes, de la administración del agente quimioterapeutico o antibiotico apropiado y de una asistencia cuidadosa. A veces es necesaria la traqueotomía. Se han presentado sugerencias relativas a las indicaciones para este procedimiento, la manera de ejecutarlo y el cuidado subsiguiente del niño operado. Se contraindican los sedativos y las drogas antihistamínicas en el tratamiento de la laringotraqueobronquitis aguda.

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# Bronchography\*

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Bronchography is an important diagnostic procedure and an essential part of a complete chest study when a diagnosis is not definitely proved by the usual history, physical examination, x-ray films and laboratory tests. Even when the diagnosis is known, information obtained from bronchograms may affect the type of therapy to be applied to certain patients.

It is the purpose of this paper to outline a simple technic which will make bronchography available to anyone who has fifteen minutes to spend with his patient and who has a fluoroscope and an x-ray machine available. Although the technic described was developed independently, it was later presented by Forrestier to the Southern Medical Association in 1937.

## *Technic*

Very little, if any, preparation of the patient is needed to make the routine or "screening" bronchograms filling both lower lobes, the right middle lobe, and the lower portion of each upper lobe. While it was once our practice to give nembutal an hour before, followed by codeine thirty minutes before the procedure, the majority of our patients now receive no medication. Only those patients who are unusually apprehensive, high strung, or uncooperative receive these preliminary drugs. It is unnecessary to withhold meals, although there is less saliva to interfere with a good filling of the bronchi if the procedure is carried out at least two or three hours after the patient has taken anything by mouth.

The equipment is simple, consisting of a 20 cc syringe to which a 3½ inch piece of Carrel rubber tube is attached, a medicine glass with eyedropper, a piece of gauze, and a cup for warming the oil under running water. The anesthetic mixture consists of approximately 10 cc of Pontocaine 0.5 per cent with 5 or 10 drops of adrenalin in it. We prefer the use of Iodochloral because its viscosity, when the oil is warmed, is just right for our purpose. Unless a large amount of the oil is swallowed by the patient, only 20 cc is used.

Anesthetization is carried out with the patient sitting in a chair

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and leaning sharply to one side or the other while his head is supported by an assistant. The patient is asked to "stick out his tongue" (dentures having been removed) and the tongue is firmly grasped between the thumb and forefinger of the operator and withdrawn to prevent swallowing. The patient is then instructed to breathe through his mouth with "full, quiet breaths" while one or two dropperfuls of the anesthetic mixture are slowly instilled into the nostril which has the freer passage. The chief difficulty to be overcome is the tendency to swallow. An attack of coughing may ensue in which case the anesthetization is repeated until the operator is satisfied that the Pontocaine-adrenalin mixture has run well down the trachea without causing irritation. The patient is then tilted to the opposite side and the process is repeated through the same nostril. During the three or four minutes consumed by the process of anesthetization, the iodized oil and the syringe are warmed by running hot water over them.

Instillation of the iodized oil is performed in essentially the same manner and through the same nostril so that the oil flows over the membranes previously anesthetized. The rate of flow is varied with the type of breathing of the patient, but averages approximately 10 cc for every two breaths.

The oil is directed into any lobe desired by placing the patient in an appropriate position as it is *instilled*. Satisfactory delineation of the bronchial tree is rarely obtained by positioning the patient *after* the filling has been completed. A little practice will make one adept at positioning the patient so that the desired bronchi will be filled. In general, a forty-five degree angle of direct lateral inclination will produce a filling of the *anterior* segments of the lower lobe, the middle lobe on the right or the lingula on the left, and those anterior branches in the upper lobes immediately above them. To obtain a filling of the superior segments of the lower lobes the patient must be tilted laterally and posteriorly. We usually start the instillation with a direct lateral inclination of the patient and gradually rotate him to a lateral and dorsal inclination.

It is possible to fill the upper lobes well by this method. When a filling of the upper segments and apex of the upper lobes is desired, the patient is seated and inclined almost horizontally in the direct lateral position, and is instructed to take *very full, deep breaths*. The warmed oil is carried into the upper bronchi in the same fashion as is inspired air, not by gravity, but by the negative pressure developed by the respiratory movement.

We do not advise an attempt to fill all the major bronchi with oil at one sitting. A very unpleasant sensation of suffocation can be developed and it is not impossible that certain patients with

impaired respiratory function and children could actually be asphyxiated. Rather, we prefer to make our routine bronchograms in such a fashion that the upper segments of each upper lobe are free of oil, to be filled at a different sitting if indicated. Or in case our preliminary examination indicates pathology in the upper lobes, we will perhaps fill all of one lung at one sitting, leaving the contralateral lung free of oil at the time.

For routine purposes the right lung is filled first in front of the fluoroscope and when the desired bronchi have been delineated a *right lateral* x-ray film is made. This will clearly outline the bronchi of the various segments without interference from shadows in the contralateral lung. It is also possible to be much more certain of the identification of various branch bronchi in the true lateral film than in the diagonal view where a portion of the bronchial tree may be partially obscured by the heart shadow.

Then in a similar fashion the left bronchi are outlined and a postero-anterior film is made. In some cases a left anterior oblique film may be useful.

Stereoscopic x-ray films of iodized oil instillations are frequently used in place of the foregoing group of films. In them it is still easier to identify the bronchus of each lobule of every lobe filled.

There are a few precautions which make the difference between good and useless bronchograms. (1) It is important that the x-ray films be made *immediately* after the instillation of oil, before there has been an opportunity for the bronchial outlines to be clouded by deposits of oil in the alveolar spaces. (2) Iodochlorol flows best and reaches its ideal viscosity when *warmed* to a little above body temperature. It is also least likely to cause the patient to cough when properly warmed. (3) The use of too much oil will obscure the structures which are being examined, namely, the bronchi. It is usually sufficient to use 10 cc. on each side.

Definition is improved by the use of a grid, either of the Bucky type or one which is stationary and can simply be hung on the cassette holder between the patient and the film. In any case the penetration must be adequate to outline the oil in the bronchi *through* the heart shadow and *through* the shadow of the diaphragm and liver. This can readily be achieved with ordinary x-ray equipment and without materially increasing the time of exposure by using its maximum capacity and, in many instances, shortening the distance from the usual 72 inches to 42 inches. The intensity of the exposure varies inversely with the square of the distance so that this change will result in approximately three times the penetration achieved by the same factors at six feet.

Immediately following the instillation of oil and the making

of x-ray films, every patient is given a postural drainage. He is further instructed to take postural drainage *three or four times more* before retiring. This is performed by assuming an angle of forty-five degrees with the floor, lying over a bed or examining table, and coughing forcefully for two or three minutes to evacuate all the oil possible. The majority of patients will be entirely free of oil by the following day. This is an important maneuver in the prevention of lipid pneumonia, atelectasis or other complications.

This is not the only effective technic for making bronchograms, and for certain special indications and in small children other technics must be followed. Excellent bronchograms in children can be made through the bronchoscope if the bronchoscopy is carried out on the x-ray table, or if a portable x-ray machine is placed in position in the bronchoscopic room during the introduction of the oil. To obtain satisfactory bronchograms it is important that the films be made immediately upon the introduction of the oil into each lung individually. All oil possible is withdrawn from each lung through the suction apparatus and the child is given continuous postural drainage with the foot of the bed elevated until the chest is clear.

Aside from an occasional patient whose salivary glands become swollen and painful as a result of sensitivity to iodine we have had no untoward results in well over two thousand sets of bronchograms made by the technic described here.

### *Indications*

When bronchography is easily and readily available, its uses are found to be more numerous. Besides the traditional use of bronchography for the identification of bronchiectasis and a determination of its distribution and extent for surgical purposes, it is an invaluable aid in tracing down the cause of hemoptysis of unexplained origin. A persistently blocked bronchus as observed on more than one bronchogram may well mean a previously unsuspected foreign body, an adenoma of the bronchus, a carcinoma or other lesion which fails to cast a shadow on the normal roentgenogram. It is also amazing to find at times how much bronchiectasis may exist, causing hemoptysis, when the patient fails to give a history of persistent cough and sputum.

Some patients suspected of having bronchiectasis from the history alone are found to have generally attenuated bronchi. The associated cough and occasional wheezing are found to be due to an allergy—asthma without marked wheezing.

In the distal bronchi which are not readily visualized with a bronchoscope, one may identify the bronchus in which a foreign

body is situated by means of bronchograms, thereby facilitating its removal bronchoscopically

In patients in whom it is difficult to differentiate areas of atelectasis from localized pockets of fluid or extrapulmonary tumor masses, bronchograms provide the indisputable differential diagnosis

A generalized density about the base of the thorax makes it impossible in some cases to tell whether or not pathology is in the lung or is located below the diaphragm and bronchograms again will provide valuable information

In tuberculosis the use of iodized oil has been attended by no untoward complications We no longer hesitate to instill iodized oil in the patient who has had tuberculous disease and who has unexpected or unexplained positive sputum Tuberculous bronchiectasis and tuberculous tracheo-bronchitis have both been demonstrated in many instances as the cause of this phenomenon

There are other special indications for bronchography If the examination can be quickly and easily performed without any particular distress to the patient, the chest diagnostician will find it one of his most useful and frequently used tools

#### SUMMARY

We have outlined a technic for bronchography which is simple, easy, and which may be carried out as an office procedure without elaborate preparation or distress to the patient It is effective for routine purposes and in the majority of cases A few of the indications for bronchography are outlined

#### RESUMEN

Hemos bosquejado una técnica para la broncografía que es sencilla, fácil y que puede llevarse a cabo como procedimiento de oficina sin preparativos esmerados o dolor al paciente Es eficaz para fines rutinarios en la mayoría de los casos Se bosquejan algunas de las indicaciones para la broncografía

# Cavity Closure following the Discontinuation of Ineffective Pneumothorax\*

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Judging by the paucity of reports of the rapid and unexpected closure of tuberculous cavities after the discontinuation of an ineffective pneumothorax is a rare occurrence. In 1938 Steele et al.<sup>1</sup> reported 12 cases in which cavities closed unexpectedly after the discontinuation of an ineffective pneumothorax. Since it is the only such report in the literature, this additional report of 11 cases seems worthwhile.

The first 5 cases were observed during a period of forty-four months in a large sanatorium. The other 6 cases, cases 6 to 11, inclusive, were seen in a recent period of 15 months in a small sanatorium (C.C.S.) with an average of 1000 tuberculous patients.

In most of our patients phrenic paralysis was substituted immediately after the pneumothorax was discontinued. In recent months phrenic paralysis has become a virtually routine procedure in cases with specific contraindications to pneumothorax. Ten of our 11 cases had phrenic paralysis. Five of these also had pneumoperitoneum. Pneumoperitoneum has not been used because in many instances the diaphragm becomes so elevated after phrenic crush that it is difficult to obviate the need for pneumoperitoneum. If the diaphragm does not rise to a high level within a period of two or three weeks, pneumoperitoneum is induced for the purpose of further relaxing the lung.

In selected patients pneumoperitoneum is an effective method in the treatment of tuberculosis. Its usefulness has not been generally appreciated. Although this is not intended as a report on the merits of pneumoperitoneum, the role of pneumoperitoneum is well illustrated by the fact that in the last eighteen months during which this form of therapy has been used, five such cases have been seen, whereas in the previous forty-four months there were only five cases.

Probably, every phthisiologist has observed patients with ineffective pneumothoraces whose lungs after reexpansion showed un-

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expected improvement characterized by resorption of exudate, decrease in size (or closure) of cavities and contraction of the diseased portion of the lung. Such rapid improvement is rarely noted in patients treated solely by bed rest. It seems paradoxical that so much improvement should follow the discontinuation of an anatomically poor and clinically ineffective short term pneumothorax.

An anatomically perfect pneumothorax produces concentric collapse, relaxation and diminution in motion of the diseased portion of the lung. Some degree of relaxation also occurs in many anatomically poor but clinically effective pneumothoraces. This relaxation and contraction assists in the resolution of foci of infiltration. These favorable changes are the basic aims of collapse therapy.

It is not the purpose of this paper to discuss the various hypotheses of cavity closure. Suffice it is to say that cavity closure depends on such factors as atelectasis, compensatory emphysema, fibrotic contraction of cavity wall and occlusion of bronchocavitary communication. It is believed that no single factor accounts for cavity closure but that several play variable roles.

Steele et al,<sup>1</sup> offered no explanation for cavity closure in their patients. The only explanation I can advance is the already known mechanisms of cavity closure which are aided by the relaxation which begins with the ineffective pneumothorax and continues with phrenic paralysis and pneumoperitoneum. It is customary in collapse therapy to date a patient's improvement from the day an effective collapse is achieved by one method or another. In view of the benefit derived from many so-called ineffectual pneumothoraces, one must admit that improvement begins and coincides with the period of so-called ineffectual pneumothorax. Conversion of sputum occurs in some so-called anatomically poor pneumothoraces. In other anatomically poor pneumothoraces sufficient relaxation occurs to permit the diseased portion of the lung to contract and occupy a smaller space. This contraction has been repeatedly observed in right upper lobe disease where the lobar fissure before pneumothorax is horizontal but after reexpansion is found to follow an ascending plane in the lateral direction, indicating contraction of the entire lobe. Further complete contraction of a badly diseased right upper lobe into the apex and against the mediastinum has been seen occasionally after discontinuation of an ineffective pneumothorax. This rapid decrease in volume of an entire lobe is attributed to the beneficial effect of the short term pneumothorax.

Even though a lung may be broadly adherent in the upper portion, unless the base is solidly adherent also, some relaxation



TABLE 1 — ANALYSIS OF ELEVEN CASES

Case	Age and Sex	Date of Admission to Sanatorium	Duration of Pneumothorax	Date of Phrenic	Time from Phrenic Crush to Cavity Closure	Pneumoperitoneum	Status on Discharge from Sanatorium	Status on Last Observation	Comment
Case 1 O F	24-F	4/16/43	2 mos	6/30/43	9 mos	No	12/5/44 Arrested	Not Traced	Closed 4 cm left apical cavity
Case 2 R A	32-F	7/22/43	6 wks	9/24/43	11 wks	No	9/4/44 Arrested	Not Traced	Closed 2.5 cm right apical cavity
Case 3 O C	21-F	10/26/42	5 wks	11/14/42	9 mos	No	4/24/44 Arrested	Not Traced	Remarkable result Closed 7.5 cm right upper lobe cavity
Case 4 D W	50-F	8/18/42	9 wks	9/27/43	12 wks	No	2/11/44 Quiescent	Not Traced	Closed 2.5 cm right upper lobe cavity
Case 5 G I	27-F	7/ 8/43	8 wks	Not done	7 mos *	No	9/5/44 Arrested	Not Traced	Closed 3 cm right upper lobe cavity
Case 6 R D	18-F	7/23/45	11 wks	11/ 1/45	9 wks	No	2/1/46 Quiescent	Arrested 3/15/47	Closed 3 cm right apical cavity
Case 7 W C	36-M	5/23/45	10 wks	5/24/45	8½ mos	Yes	11/10/46 App Arres	Arrested 3/15/47	Closed 4 cm left apical cavity
Case 8 D H	26-F	5/27/46	2 wks	6/17/46	5 mos	Yes	Still in Sanatorium	Sputum Neg Doing well	Has diabetes Closed 4 cm left apical cavity
Case 9 B C	16-F	4/ 9/46	2 wks	7/ 6/46	6 mos	Yes	Still in Sanatorium	Sputum Neg Doing well	Closed 4 cm right apical cavity
Case 10 C D	24-M	10/18/45	8 wks	12/27/45	10 mos	Yes	Still in Sanatorium	Sputum Neg Doing well	Closed 5.5 cm right upper lobe cavity
Case 11 A M	31-M	6/ 4/46	3 wks	7/ 3/46	5½ mos	Yes	3/18/47 App Arres	Apparently Arrested	Closed 4.5 cm right apical cavity

\*Seven months from induction of pneumothorax

occurs in an apico-basal direction. When the patient is in bed, the pull of gravity is overcome in an apico-basal direction allowing the lung to retract upward. Pneumothorax more or less releases the lung from the pull of the diaphragm. Phrenic paralysis and pneumoperitoneum further the upward retraction of the lung.

Cavity closure requiring several months may not be considered rapid by some but the closure of cavities in Cases 2 and 4 in a few weeks seems significant, particularly in Case 4. This patient had a persistent 2.5 cm cavity for several months but refused pneumothorax. She finally agreed to the induction of a right pneumothorax but the collapse was ineffective because of dense pleural adhesions. Twelve weeks elapsed from the date of induction to complete reexpansion of the lung, following which the cavity was found closed and remained so. This case illustrates more than any other the beneficial effect of a short term ineffective pneumothorax.

No case with cavity smaller than 2.5 cm in diameter is included in this group. The shortest cavity closure time seen was in Case 2 in which a 2.5 cm cavity closed in eleven weeks. The largest cavity (Case 3) measured 7.5 cm in diameter and closed in nine months. Smaller cavities in other cases required a longer time to close. In general, there was no correlation between the size of the cavity and the length of time required for closure. Most of the cavities were of recent origin, the walls were not thick and no doubt belong to Pinner's Type 2. None were Pinner's Type 3. In all cases the sputum remained positive two to three months after the cavity closed. In eight of the patients the cavity was located in the right upper lobe while in three it was in the left upper lobe.

The general condition on admission of the 11 cases listed in Table 1 was better than average. An unusual feature which is not brought out in the table is that the contralateral, or so-called good lung, in all except 3 cases, showed no roentgenographic evidence of disease. In these 3 cases there was minimal exudative disease which regressed satisfactorily. The clinical and radiographic progress of these patients has been excellent.

Because of the frequency with which empyema complicates ineffective pneumothorax, early discontinuation has been the rule in our work. Eleven weeks was the longest pneumothorax trial period in these cases and there were no complications.

### SUMMARY

Eleven cases illustrating the closure of tuberculous cavities following the discontinuation of ineffective pneumothorax have been tabulated and analyzed.

Phrenic paralysis was substituted for the pneumothorax in 10 of the 11 cases Pneumoperitoneum supplemented phrenic paralysis in 5 cases Phrenic paralysis and pneumoperitoneum were effective adjuncts in the treatment of these cases

Certain principles of collapse therapy and their influence on cavity closure in these cases are discussed

Cases 6 to 11 inclusive have been followed since this paper was submitted for publication At this time all have arrested disease

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I wish to thank Dr G E Gwinn, Superintendent, Pinecrest Sanatorium, Beckley, West Virginia, for the privilege of reporting Cases 1 to 5 inclusive, which I observed while a member of his staff

### RESUMEN

Se han presentado en forma de tabla y se han analizado 11 casos que ejemplifican el cierre de cavernas tuberculosas subsiguiente a la discontinuación de neumotóraces ineficaces

En 10 de los 11 casos se reemplazó al neumotorax con la parálisis del frénico En 5 casos el neumoperitoneo reforzó la parálisis del frénico La parálisis del frénico y el neumoperitoneo fueron adjuntos eficaces en el tratamiento de estos casos

Se discuten ciertos principios de la colapsoterapia y la influencia que ejercieron sobre el cierre de las cavernas en estos casos

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# Pleural Fibrin Body Simulating Cardiac Aneurysm Report of a Case

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In recent years, roentgenologic study has come to be recognized as the most accurate method in the diagnosis of left ventricular aneurysm<sup>1-6</sup> Generally there is an abnormal contour of the cardiac shadow with a localized bulge somewhere along the ventricular border A paradoxical pulsation at the site of the aneurysm may be helpful but it is not always present The apex of the heart is said to be the most frequent location for aneurysms but this type may be most difficult to detect due to the fact that the abnormal ventricular bulge is partially hidden by the shadow of the left diaphragm Films taken in deep inspiration may be of some help Emphasis has justly been placed on the importance of fluoroscopy in the proper evaluation of an abnormal cardiac silhouette This is true not only in the identification of various types of heart lesions but also in their differentiation from noncardiac disease

The case reported below showed a localized shadow in the region of the cardiac apex which resembled a ventricular aneurysm However, fluoroscopy showed that the suspicious density was caused by a large fibrin body which had lodged at the bottom of the left pleural space so that it seemed to be continuous with the cardiac shadow

## CASE REPORT

R.T.A., a 37-year-old white male was transferred from another institution for treatment of his tuberculosis He had worked as a jeweler for 17 years and had always been in good health until one year ago when he noted the onset of cough, slight dyspnea and easy fatigue while he was with the U.S. Army in Europe In July, 1946 he had a ten-ounce hemoptysis and roentgenograms of the chest at a Veterans Administration hospital showed a tuberculous process in the left upper lobe with a 3-centimeter central area of increased translucency which was interpreted as a cavity Pneumothorax was instituted in September, 1946 although no definite tubercle bacilli had been isolated from the sputum He was transferred to the Veterans Administration Hospital, Oteen, North Carolina on September 24, 1946

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\*From the Department of Medicine and Surgery, Veterans Administration Oteen North Carolina published with permission of the Chief Medical Officer Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author



FIGURE 1

FIGURE 2

FIGURE 3

*Figure 1* Admission film of September 24, 1946 demonstrating abnormal shadow in the region of the cardiac apex. Arrow indicates the small incisura separating the oval density from the normal left cardiac border—*Figure 2* Right anterior oblique view of chest showing large egg-shaped fibrin body in left pleural space (indicated by arrows)—*Figure 3* Pre-pneumothorax chest film of patient, dated August 23, 1946 showing cardiac shadow of normal size and shape

His admission chest film (Fig 1) at this hospital showed a pneumothorax on the left side with about 25 per cent collapse of the left lung and a minimal amount of fluid in the left costophrenic sulcus. Dense infiltration was present in the medial portion of the left upper lobe just above the hilar vessels. No definite cavities were seen. Right lung was clear.

The cardiac silhouette was abnormal with a convex density adjacent to the cardiac apex and separated from it only by a small incisura. The appearance was suggestive of an aneurysm of the apex of the heart. However, this patient gave no history of any preceding coronary occlusion or any definite symptoms of heart disease. Auscultation over the precordium was essentially negative and the blood pressure was 120/82. Electrocardiogram was normal.

The patient was fluoroscoped in various positions and it was found that the abnormal shadow adjacent to the cardiac apex was caused by a large egg-shaped fibrin body resting in the antero-medial portion of the left pleural sac at the level of the cardiac apex. This is well demonstrated in the right anterior oblique view of the chest (Fig 2).

The chest film done on this patient before induction of pneumothorax was later secured from the institution where he had originally been hospitalized. It showed a heart shadow of normal configuration. The abnormal density at the apex had apparently developed only after the induction of the pneumothorax (Fig 3).

Pleural fibrin bodies are known to develop in a certain percentage of pneumothorax cases. Some authorities regard injury to an intercostal vessel or tearing of an adhesion band as a prerequisite to the formation of fibrin bodies. However, there are cases in which the fibrin body seems to develop within a pleural exudate with no definite history of a traumatic episode. In such cases there is usually present an appreciable amount of pleural fluid before the fibrin body makes its appearance. Usually a fibrin body will move freely in the pleural exudate when the patient is postured and will thus be easily identified on fluoroscopy. Once it becomes adherent, however, either to the diaphragm or to the wall of the pleural cavity, diagnosis becomes much more difficult.

### SUMMARY

A case is reported in which a large fibrin body lodged in the left pleural space in such a position as to simulate an aneurysm of the apex of the heart on the postero-anterior film of the chest. Fluoroscopy and oblique projection, together with comparison of pre-pneumothorax roentgenogram revealed the true nature of the condition.

### RESUMEN

Se informa sobre un caso en el que un cuerpo grande de fibrina paró en el espacio pleural izquierdo en tal posición que, en la película postero-anterior del pecho, aparentó ser un aneurisma.

del vértice del corazon El examen radioscópio y la proyección oblicua, comparados con una radiografía tomada antes de comen-zarse el neumotórax, revelaron la verdadera naturaleza del caso

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# A New Mirror-Cannula for Laryngo-Tracheo-Bronchial Anesthesia, Medication, or Instillation of Opaque Oils

A ALBERT CARABELLI, M.D., F.A.C.P., F.C.C.P.\*  
Trenton, New Jersey

Frequently there comes to the laryngologist, bronchoscopist, and pulmonologist a desire to possess three hands. This is especially true during the process of anesthetizing the larynx, trachea, or bronchi. The usual procedure is to hold the mirror in one hand, the cannula in the other, using the patient or an assistant to make traction on the tongue. This means a total of three hands about the mouth orifice. Traction of the tongue by an assistant or the patient has a considerable personal variable which ranges from too much traction resulting in pain and gagging to too little resulting in almost complete block of the line of vision for the operator by the elevation of the dorsum of the tongue. If the patient holds the tongue, there is a constant tendency to retract it into the mouth even with the most cooperative patient. Manipulative dexterity on the part of the operator has in many cases developed skills that make anesthesia of the larynx and trachea relatively simple procedures. On the other hand some operators even after many years find this procedure cumbersome and occasionally awkward, especially with certain types of patients. Occasionally the tension during this procedure has been such that an unsuccessful anesthesia has resulted or the patient has become unwilling to continue with the ordeal.

In view of the personal difficulties with the old procedure which seem inherent in the method, the author has attempted to simplify the procedure of laryngo-tracheo-bronchial anesthesia by eliminating the use of the third hand and by making other refinements which result in a rather smooth technique without at any time obstructing the line of vision. This was done by devising a simple mirror-cannula which is described below. Proficiency in the use of this cannula comes rapidly, and at present what was once an ordeal with certain patients has become a matter of routine. With the use of the mirror-cannula complete control is had at all times on the degree of traction of the tongue and the solution is instilled accurately and economically where intended.

Prior to developing the mirror-cannula, consideration was given

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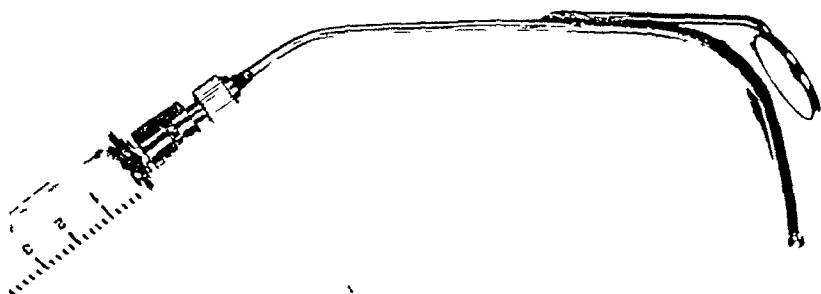


to the ideal requirements for successful and simple anesthesia of the larynx, trachea, and bronchi. It was decided that were a single instrument designed that would permit conformance with the following requirements, an ideal instrument for this procedure could be evolved

- 1) A procedure that could be performed by the operator alone without the assistance of the patient or nurse
- 2) Lack of bulk to the instrument for easy introduction into the mouth without eliciting undesirable reflexes
- 3) Design of such an instrument to closely follow the natural oro-pharyngeal curve without touching too many structures in the mouth, pharynx or larynx
- 4) Incorporation into the instrument of a means of holding back the flaccid uvula so that it did not fall unto the mirror and obstruct the line of vision
- 5) An instrument that permits an unobstructed view at all times of the posterior portion of the epiglottis and of the vocal cords
- 6) An instrument that permits complete control of the solution to be instilled under constant visual guidance

After much experimentation, mostly by the trial and error method, a mirror-cannula was developed that permitted the above desiderata. Such a cannula is illustrated in Figure 1. The basic parts consist of a stock laryngeal mirror (No. 4) and an Abraham laryngeal cannula of malleable metal. The shortened shank of the mirror is simply soldered to the back of the cannula after molding by hand to the required shape. Multiple clinical trials finally evolved a mirror-cannula with specifications which were considered generally satisfactory without further modification for anesthesia of the larynx, trachea, or bronchi. The following are the specifications for the mirror-cannula.

- 1) Size of mirror: Number 4 laryngeal mirror, boilable
- 2) Length of shank of mirror: 4.5 cm from edge of attachment to mirror



- 3) Angle of mirror to the horizontal line 45 degrees
- 4) Angle of hub of cannula to the horizontal line 30 degrees
- 5) Angle of the descending portion of the cannula to the horizontal line 110 degrees
- 6) Distance from the center of the mirror to the curve of the cannula 0.5 cm
- 7) Distance from the center of the mirror to the rounded tip of the cannula 3.5 cm

The angle of the mirror to the shank is changed to conform with specification number 3, above, as the original angle with which the mirror comes is not the same. Changing of this angle is made close to the edge of the attachment of the shank to the mirror with the aid of a narrow-nose wire-bending pliers so as not to crack the glass.

Experimentation with sizes 1 to 6 of the laryngeal mirror, but using the same basic specifications proved that the ideal size of mirror was a number 4. The smaller sizes permitted the uvula to occlude vision when it slipped over the anterior portion of the mirror. The larger sizes were found too bulky for introduction and gave an unnecessarily large view of the vocal cords and the surrounding structures.

Variations of the length of the tip, keeping the other specifications constant also revealed enough difficulties to warrant standardization to the 3.5 cm length of the tip. Shorter distances may be used but have the disadvantage that the tip cannot be placed over the posterior portion of the epiglottis so as to direct the solution between the vocal cords. Generally it was found that with the shorter tips the solution trickled down the anterior portion of the epiglottis and traveled into the pyriform sinuses eliciting a swallowing reflex which made for loss of the solution into the esophagus and failure to anesthetize the larynx. Another disadvantage was that the epiglottis could not be engaged by the tip of the cannula and thus secure its position just above the vocal cords. Longer distances than 3.5 cm also had several disadvantages. One was that the tip of the cannula became captured between the vocal cords before they could be anesthetized and caused spasm, cough, and gagging. Another disadvantage was that introduction of the longer tip into the natural oro-pharyngeal curve was cumbersome and evoked gagging and salivation.

The 3.5 cm length of the tip was found to be ideal since it permitted easy introduction into the mouth along the natural oro-pharyngeal curve with only two points of contact: the uvula and the upper, posterior portion of the epiglottis. Since these structures are usually well anesthetized by the preliminary spraying with an atomizer, no undesirable reflexes are elicited when they are touched by the cannula. The posterior portion of the mirror is used to

gently push back the flaccid uvula thus keeping it out of the field of vision and the tip is made to rest gently against the upper posterior portion of the epiglottis at such an angle that the vocal cords are well visualized, permitting the solution to be dropped directly upon them or between them at will without setting up the severe reflexes noted when the tip touched the cords or lies between them

Attached to the mirror-cannula is a standard Luer-lock syringe which contains the solution to be used. The angulation of the hub is such that vision is not impeded at any time by the bulk of the syringe and has the added advantage that the hand can be kept at a low position and is not in the line of vision.

A feature worthy of mention of this mirror-cannula is that since the tip is also malleable its angle with the horizontal may be changed to suit the occasional patient who has the epiglottis at an angle varying from the normal. By manual angulation of the tip, introduction behind the epiglottis can be accomplished with almost any anatomical variation of the epiglottis. This contingency is apparently rather rare and the degree angle of the tip was changed only once in a series of 180 anesthetizations.

Use of the mirror-cannula, of course, presupposes preliminary anesthetization of the oro-pharyngeal and superficial laryngeal structures with a spray anesthesia from an atomizer as is done with the usual method. Fogging of the mirror is also controlled by heating in the flame of a spirit lamp or hot water.

### SUMMARY

1) A simple indirect vision mirror-cannula is described which simplifies laryngo-tracheo-bronchial anesthesia, and instillation of medication or opaque oils.

2) The mirror-cannula is simply constructed of standard parts and can be easily and expeditiously assembled.

3) Use of the mirror-cannula obviates the use of the patient or an assistant to make traction on the tongue.

4) The optimum specifications for such a mirror-cannula are described.

### RESUMEN

1) Se describe un sencillo espejo-canula de visión indirecta que simplifica la anestesia laringo-traqueo-bronquial y la instalación de medicinas o aceites opacos.

2) Se construye sencillamente este espejo-canula, usando partes regulares que se pueden armar fácilmente y con prontitud.

3) Con el empleo del espejo-cánula no se necesita que el paciente o un asistente halen la lengua.

4) Se describe la mejor manera de construir el espejo-cánula.

# Sociedad Argentina de Tisiologia

RODOLFO E CUCCHIANI ACEVEDO, M.D  
Secretary

The Executive Committee of the Sociedad Argentina de Tisiologia appointed Dr Oscar P Aguilar, Dr Juan R Paso, and Dr Rodolfo Cucchiani Acevedo as a permanent committee to investigate the use of streptomycin in tuberculosis, and the following statement is made as a result of their study

"Special sessions of the Sociedad Argentina de Tisiologia, held on October 23, and 24, 1947, were devoted to the question of streptomycin in the treatment of tuberculosis. The 'clinical protocol' presented at this meeting and the results published in the Primer Congreso Argentino de Tisiologia agree with the experience of the men in other countries, especially the United States. The results of this investigation are as follows

1) Streptomycin represents a real advance in the treatment of tuberculosis, however, the effectiveness of this drug is variable and depends upon such factors as the type of disease, the stage of activity, whether it is a pulmonary or an extrapulmonary disease

2) The use of this drug is too recent to evaluate properly, from the standpoint of lasting effect, the results obtained from streptomycin therapy

3) The results obtained in the treatment of tuberculous meningitis are sufficiently promising to advocate the early and intensive use of streptomycin by the intramuscular and intrathecal method in all patients in whom the clinical diagnosis of tuberculous meningitis have been made

4) Streptomycin should also be used parenterally in cases of acute miliary tuberculosis and in cases of hematogenous dissemination that precedes chronic tuberculosis with foci in various organs

5) Streptomycin is effective in the treatment of fistulae of tuberculous origin

6) Results obtained from streptomycin therapy in tuberculous lesions of the larynx, bronchus or trachea are encouraging. Similar results have been observed in patients with ulcerative lesions of the digestive tract

7) Use of streptomycin is justified in the acute forms of pulmonary tuberculosis. However, this is not always the case in

pneumonic or bronchopneumonic episodes that occur in advanced cases of chronic pulmonary tuberculosis

8) Streptomycin is not effective in the treatment of fibrous or fibrocaceous chronic pulmonary tuberculosis and should not be used in such cases. The use of streptomycin is also contraindicated in early cases of tuberculosis that are amenable to other, recognized forms of therapy because of the toxicity that accompanies the use of this drug

9) In general, streptomycin is an adjunct to, and does not take the place of therapeutic measures of proved effectiveness in pulmonary tuberculosis. Thus, it may be considered as an adjunct to collapse therapy, particularly when an inflammation of the bronchus interferes with cavity closure

10) It is effective as a preventive and curative measure in post-operative tuberculous complications

11) Streptomycin seems to be destined to expand the range of indications for collapse therapy and surgical treatment of tuberculosis

12) It is advisable that streptomycin should be used under the control of the phthisiologist as much as possible "

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#### CORRECTION IN THE JULY-AUGUST ISSUE

In Dr A J Steiner's Discussion of Dr C C Macklin's article, "Respiratory Volume Changes in the Pulmonary Blood Vessels in Relation to Artificial Relaxation Therapy," on page 548, the percentages given were incorrectly printed. It should have read, "The areas of two pulmonary arteries increased on inspiration, a large one increased 35 per cent, and a smaller one increased 40 per cent "

# EDITORIAL

## 'Diseases of the Chest' Now Published Monthly

With this issue *Diseases of the Chest* becomes a monthly publication. During the past few years the demand of authors for the publication of their papers became so great that a large backlog of manuscript accumulated. Not infrequently papers were published almost two years after they were accepted. Moreover, many good papers were returned to their authors because of lack of space in the Journal. This posed a serious and embarrassing problem for the Editorial Board. Although the number of pages was increased from 610 in 1946 to 750 in 1947, and 950 in 1948, the demand continued to far exceed our ability to publish within a reasonable time. Therefore, on June 17, 1948 the Editorial Board proposed that a serious effort be made to arrange for monthly publication of the Journal, beginning with the January, 1949 issue. The Board of Regents carefully considered this proposal and voted favorably on June 20th.

In the future, as in the past, every effort will be made to choose papers on the basis of such factors as timeliness, presentation of new facts, procedures, etc. The return of a manuscript to its author will not necessarily mean that it is unworthy of publication, it may be rejected because other papers have been accepted or recently published on the same or closely related subjects, etc. It is desirable to produce a well balanced journal.

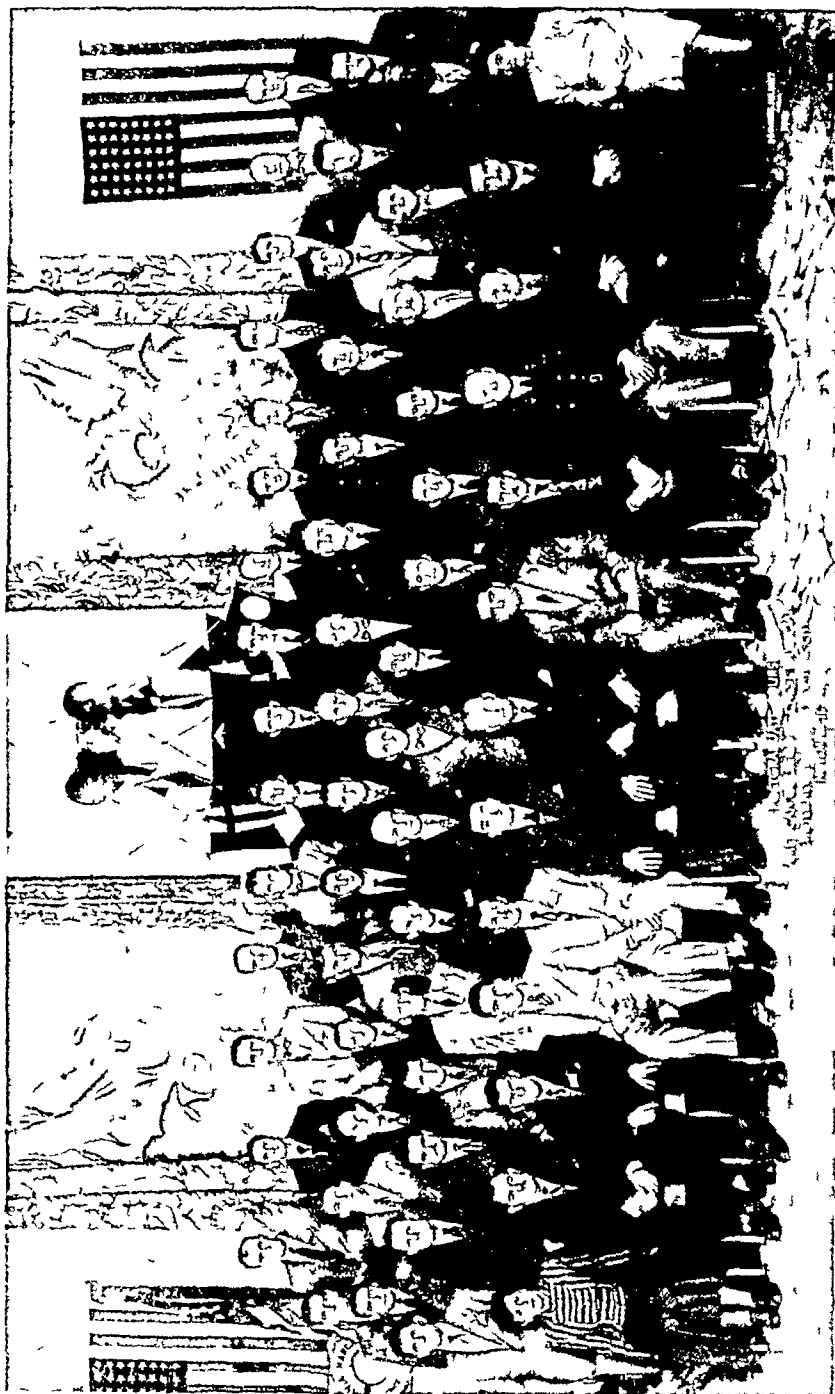
*Diseases of the Chest* is the medium through which members of the American College of Chest Physicians and others throughout the world present the results of their investigations to physicians and scientists everywhere. It is the medium through which diagnostic, therapeutic and preventive measures are presented and evaluated, and through which members of the numerous College Chapters and chest physicians throughout the world keep in touch with one another. Thus they are knitted into one large family, each member of which takes pride in the accomplishment of the others, and all are striving to relieve the sick and maintain good health among the peoples of the world, wherever they are and wherever they may be.

In its endeavor to make *Diseases of the Chest* a good medium, the Editorial Board has had the unqualified support and confidence of the members of the College and many others. With more space now available for communications in the Journal, they are desirous of not only maintaining previous standards but also elevating them with every opportunity. To this end the Editorial Board solicits criticism, suggestions and advice from physicians everywhere.

J A M

## POSTGRADUATE COURSE IN DISEASES OF THE CHEST, AMERICAN COLLEGE OF CHEST PHYSICIANS

November 8-13, 1948, Hotel New Yorker, New York City



Some of the physicians and instructors who participated in the Postgraduate Course in Diseases of the Chest of the American College of Chest Physicians

## Fifteenth Annual Meeting American College of Chest Physicians

The Fifteenth Annual Meeting of the American College of Chest Physicians will be held at the Ambassador Hotel, Atlantic City, New Jersey, June 2 through 5, 1949, just prior to the annual meeting of the American Medical Association June 6 through 10. Members are urged to make their hotel reservations at once by writing to the Executive Offices of the College 500 North Dearborn Street, Chicago 10 Illinois, giving their arrival and departure dates as well as the type of accommodations desired. A limited number of rooms are available at the Ambassador Hotel for members wishing to remain for both meetings.

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## Second Annual Postgraduate Course in Diseases of the Chest to be Given in Philadelphia

The Second Annual Postgraduate Course in Diseases of the Chest sponsored by the Council on Postgraduate Medical Education and the Pennsylvania Chapter of the American College of Chest Physicians and the Laennec Society of Philadelphia will be presented during the week of February 28 - March 5, at the Warwick Hotel, Philadelphia, Penna.

Tuition fee for the course is \$50.00 and registration, although limited in number, is open to all physicians. Application for the course may be made to the American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois. Applications will be accepted in the order in which they are received. See front advertising page vi for application form.

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## VIII Congreso Pan-Americano de la Tuberculosis (ULAST)

*Mexico City Mexico*

JANUARY 23 - 29, 1949

The following are the main themes of ULAST

- 1) Influencia del Trabajo en el origen y desarrollo de la tuberculosis
- 2) Balance de la Terapeutica quirurgica en la Tuberculosis pulmonar
- 3) Estudios sobre la funcion cardio respiratorio en la tuberculosis

### THIRD NATIONAL CONGRESS OF TUBERCULOSIS AND SILICOSIS

In conjunction with ULAST the Third National Congress of Tuberculosis and Silicosis will take place in the National Institute of Cardiology, Mexico City, Mexico during January 23-29, 1949. The following are the officials of the Congress:

President Dr. Alejandro Celis, Vice-President Dr. Juan B. Meana, Secretary, Dr. Ermilo Esquivel. The Honorary Presidents are as follows: Lic. Miguel Aleman, President of the Republic of Mexico, Dr. Rafael P. Gamboa, Secretary of Public Health, and Lic. Manuel Ramirez Vasquez, Secretary of Labor.



*Sections of the Third National Congress of Tuberculosis and Silicosis*

- 1) Epidemiologia y Profilaxis de la Tuberculosis  
Pres Dr Manuel Beltran del Rio  
Sec Dr Rafael Senties
- 2) Colapso gaseoso y tratamiento medico de la Tuberculosis pulmonar  
Pres Dr Manuel Nava  
Sec Dr Jose Ramirez Cano
- 3) Tratamiento quirurgico de la Tuberculosis Pulmonar  
Pres Dr Alfonso Aldama  
Sec Dr Rodolfo Gil
- 4) Localizaciones extrapulmonares de la Tuberculosis  
Pres Dr Alejandro Castanedo  
Sec Dr Javier Lomeli, Dr Ernesto Escalona, Dr Arturo Novoa
- 5) Padecimientos Respiratorios no Tuberculosos  
Pres Dr Manuel Diaz Estua  
Sec Dr Carlos Jimenez Caballero
- 6) Neumoconiosis  
Pres Dr Jorge Karam  
Sec Dr Javier Garcia Luna
- 7) Anatomia Patologica y Laboratorio de la Tuberculosis Pulmonar  
Pres Dr Arsenio Gomez Muriel  
Sec Dr Maximiliano Salas
- 8) Clinica y Radiologia de la Tuberculosis Pulmonar  
Pres Dr Horacio Rubio Palacios  
Sec Dr Rogelio Bolaños

The Executive Offices of the College will be pleased to assist in arrangements for those members who desire to attend ULAST and the Third National Congress of Tuberculosis and Silicosis

## COUNCIL ON RESEARCH

Charles M Hendricks M D , El Paso, Texas, General Chairman

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J Winthrop Peabody, M D , Washington, D C  
J C Placak, M D , Cleveland, Ohio  
Paul A Turner, M D , Louisville, Kentucky

## College Chapter News

### CUBAN CHAPTER

The Cuban Chapter of the College met in Havana on November 25 and elected the following officers for the coming year

Francisco J Menendez M.D , Havana, President

R Sanchez Acosta M D , Havana, Vice-President

Carlos Barroso, M.D , Havana, Secretary-Treasurer

The meeting was attended by Dr Octavio Rivero, Governor, Dr Gustavo Aldereguia, Dr Francisco J Menendez, Dr Alfredo Antonetti, Dr Orfilio Suarez Bustamente, Dr R Sanchez Acosta, Dr Rene G Mendoza, and Dr Antonio Navarrete, Regent of the College for Cuba

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### ILLINOIS CHAPTER

The Illinois Chapter of the College sponsored a dinner and scientific meeting at the Congress Hotel, Chicago, on Friday evening, December 10 A symposium on "Problems in the Management of Asthma" was presented in which the following physicians took part

"Allergic Aspects," Leon Unger, M.D , F C C.P , Chicago

'Psychosomatic Aspects," George C Hamm, M.D , Chicago

"Physiologic Aspects" Edwin R Levine, M.D , F C C.P , Chicago

The program was followed by an open discussion in which all physicians present participated

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### MEXICAN CHAPTER

The annual meeting of the Mexican Chapter was held in Mexico City on December 1, 1948 The following officials were elected to serve in 1949

Ismael Cosio Villegas, M.D , Mexico City, President

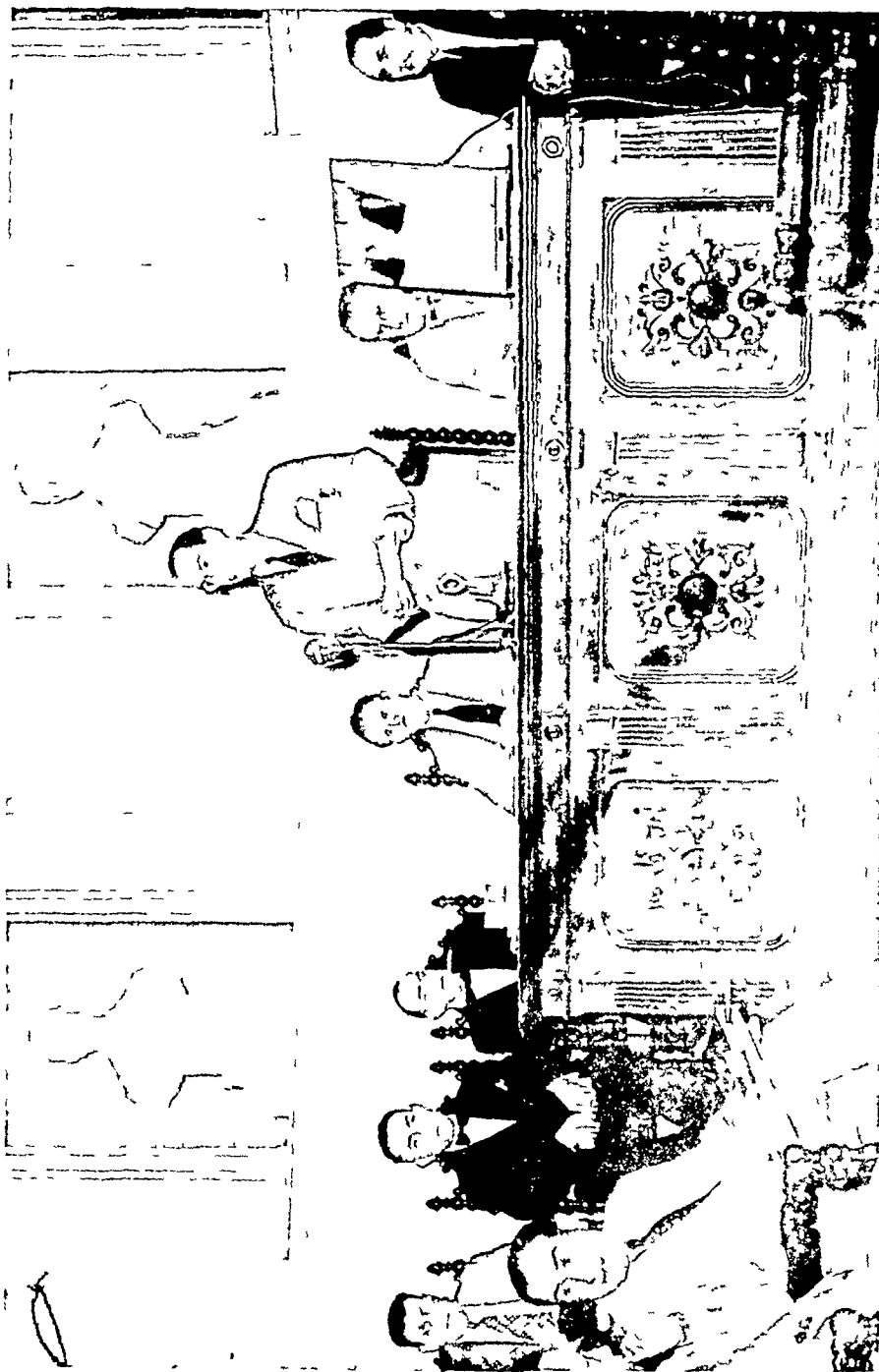
Miguel Jimenez, M.D , Mexico City Vice-President

Horacio Rubio Palacios, M.D , Mexico City, Secretary-Treasurer

A committee for the study of the By-Laws of the Mexican Chapter was appointed Dr Manuel Alonso and Dr Miguel Jimenez will comprise the committee

A Board of Examiners, consisting of Dr Fernando Rebora and Dr Carlos Noble, has been organized to pass upon all applicants applying for Fellowship in the College

The chapter resolved to lend its fullest support to the VIII Pan American Congress on Tuberculosis which is being held in Mexico City, January 23-29, 1949



*At Speaker's Table* Antonio Navarrete, M.D., F.C.C.P., Havana, Regent of the College for Cuba, (standing) Rene G. Mendoza, M.D., Havana, Chairman of the Program Committee, Cuban Chapter, Louis Mark, M.D., F.C.C.P., Columbus, Ohio, First Vice-President of the College, Octavio Rivero, M.D., Havana Governor of the College for Cuba. Seated at left, background Mr. Murray Kornfeld, Chicago, Illinois, Executive Secretary of the College, Juan R. Herradora, M.D., F.C.C.P., Jersey City, New Jersey Secretary, Council on Pan American Affairs, and Edgar Davis, M.D., F.C.C.P., Washington, D.C. member Council on Pan American Affairs of the College

### PHILIPPINE CHAPTER ORGANIZED

On November 21 the Philippine Chapter of the College was organized in Manila Gumersindo Sayago, M.D, F C C P, Cordoba, Argentina, Regent of the College for Argentina who was visiting in the Philippine Islands on a Medical Mission sponsored by the World Health Organization and the Unitarian Service Committee, participated in the organizational meeting The following officers of the 36th College chapter were elected

Miguel Cañizares, M.D, Manila, President  
Wenceslao Vitug, M D Manila Vice-President  
Fidel R. Nepomuceno, M.D Manila, Secretary-Treasurer  
Jose Avellana, M.D, Manila Counsellor

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### WISCONSIN CHAPTER

The Wisconsin Chapter of the College sponsored a program on diseases of the chest before the Vernon County Medical Society which met at Westby on Friday, August 27, 1948 The program presented was as follows

The Modern Treatment of Cough "  
Andrew L. Banyai, M D, F C C P, Milwaukee, Wisconsin  
"Diagnosis of Diseases of the Chest,"  
Leon H. Hirsh, M.D, F C C P, Milwaukee, Wisconsin

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## College News Notes

Ross K. Childerhose, M.D, F C C P, Harrisburg, Pennsylvania, presented a lecture on the "Principles and Treatment of Pulmonary Tuberculosis" by invitation to the members of La Societe de Phtisiologie de Montreal, Canada, on Tuesday, October 26, 1948

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The Metropolitan Washington Tuberculosis Conference for 1948 convened at Glenn Dale Sanatorium, October 28 College members who participated in the program were Brian B. Blades M.D, F C C P, Charles P. Cake, M D, F C C P, Daniel L. Finucane, M D F C C P, and A. Barklie Coulter, M.D, F C C P

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Leon H. Hetherington M.D F C C P Assistant Professor of Medicine at the University of Pittsburgh School of Medicine, has been appointed chief of the division of tuberculosis services of the Maryland State Department of Health Dr. Hetherington will take over direction of Maryland's four tuberculosis sanatoriums

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Sir Alexander Fleming, Honorary Fellow of the College attended a meeting of the Medical Society of London on October 25 for a discussion on streptomycin Dr. Jenner Hoskin presided Sir Alexander Fleming stated Certain results indicated that given by the mouth, streptomycin

had a rapid effect in infantile diarrhoea. It was a local action, no big dose need be given. This might turn out to be a very important use for this drug."

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Juan R. Herradora, M.D., F.C.C.P., Jersey City, New Jersey, Secretary of the Council on Pan American Affairs of the College, was invited to visit Guatemala as a guest of that country. Dr. Herradora visited Guatemala City during the latter part of October. Upon arrival he was greeted by the President of Guatemala and the Secretary of Public Health.

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At the request of the Philippine Government, the World Health Organization, Interim Commission, and the Unitarian Service Committee jointly sponsored a Medical Mission to the Philippine Islands to give lectures and conduct demonstrations on recent advances in certain fields of medical science as indicated by the Philippine Government. The Mission consisted of five members, including Gumersindo Sayago, M.D., F.C.C.P., Cordoba, Argentina, Regent of the College for Argentina. Before returning to his home in Cordoba, Dr. Sayago is visiting in the United States.

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On August 16th, the sixth session of the Australasian Medical Congress (British Medical Association) was formally opened in Perth. W. B. Cotter Harvey, M.D., F.C.C.P., was President of the Section on Public Health, Tuberculosis and Tropical Medicine. On August 20th, a public meeting was held at which the first steps were taken to form an Australian Tuberculosis Association. Among officers elected to the Association were the following College members: Dr. R. W. Cowan, M.D., F.C.C.P., Adelaide; W. B. Cotter Harvey, M.D., F.C.C.P., Sydney; and Sir Sidney Sewell, F.C.C.P., Melbourne.

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#### BACK ISSUES OF THE JOURNAL IN DEMAND

The following back issues of the journal are in demand. One dollar will be paid for each of the issues listed below upon receipt at the executive offices of the American College of Chest Physicians in Chicago:

- Volume IX, Nos. 1, 2, 3, 4 (1943)
  - Volume X, Nos. 1, 2, 3, 4, 6 (1944)
  - Volume XI, Nos. 1, 2, 3 (1945)
  - Volume XII, Nos. 1, 2, 3, 4, 5, 6 (1946)
  - Volume XIII, Nos. 1, 2 (1947)
  - Volume XIV, No. 1 (1948)
- 

#### POSTGRADUATE COURSE IN BRONCHESOPHAGOLOGY

The University of Illinois, Department of Otolaryngology, will offer a two week Bronchoesophagology Course under the direction of Paul H. Holinger, M.D., F.C.C.P., from February 7 through February 19, 1949. The tuition and laboratory fee is \$150.00 and applications can be obtained by writing to the University of Illinois, Department of Otolaryngology, 1853 West Polk Street, Chicago 12, Illinois.

## TWENTY-FIRST ANNIVERSARY YEAR OF HAROFE HAIVRI

The appearance of Volume I—1948 of the *Harofe Hawri*, The Hebrew Medical Journal, inaugurates the 21st successful year of its publication under the editorship of Moses Einhorn, M.D. The Journal's contents are not confined to technical medical topics but is divided into several sections covering a variety of related subjects of interest to the medical profession.

The original articles are summarized in English to make them available to those who are unable to read Hebrew. For further information, communicate with the editorial office of the Hebrew Medical Journal, 983 Park Avenue, New York 28, New York.

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## ANNUAL SESSION, AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians will conduct its 30th Annual Session at New York, N. Y., March 28 through April 1, 1949. Dr. Franklin M. Hanger, Jr., of New York City is the Chairman for local arrangements and the program of Clinics and Panel Discussions. The President of the College, Dr. Walter W. Palmer, Director of The Public Health Research Institute of the City of New York, Inc., and Professor Emeritus, Columbia University College of Physicians and Surgeons, is in charge of the program of Morning Lectures and afternoon General Sessions.

Secretaries of medical societies are especially asked to note these dates and, in arranging meeting dates of their societies, to avoid conflicts with the College Meeting, for obvious mutual benefits.

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## BINDING FOR COMPLETED VOLUMES

We are pleased to announce that The Book Shop Bindery, 308 West Randolph Street, Chicago, Illinois, will produce a well-bound volume at as low a price as possible for those members and subscribers who wish to preserve their issues of "Diseases of the Chest." They will bind the six issues of Volume 14 in the best grade of washable buckram with gold stamping on the spine and the member's or subscriber's name in gold on the front cover. Please send the six issues to Chicago by express or parcel post prepaid with check or money order for \$2.75 made payable to The Book Shop Bindery. The bound volume will be returned with transportation prepaid by the bindery.

## Book Reviews

*Zinsser's Textbook of Bacteriology* By David Smith and Donald S. Martin, et al, Duke University School of Medicine Cloth Price \$10 00  
Pp 992, Illustrated Appleton Century Crofts, New York, 1948

In 1935 there appeared, from the pen of Hans Zinsser, a book "Rats, Lice and History" which was the life history of typhus fever. In this book there was a lucid, simple and fascinating story of the effect of infections on, and the transmission of infectious diseases to the population, and the impetus it had on civilization. In 1940 Zinsser's last publication, "As I Remember Him," appeared. This, the reader will recall, was in essence an autobiography of Hans Zinsser. From these books one readily concludes that here was an author of first magnitude, a scientist of international reputation, and an authority in his particular field—bacteriology and public health.

For many years before the above mentioned books appeared, Zinsser's contribution to bacteriology was known to every medical student through his texts, first, with Professor Hiss (published in 1910), later published under his name alone, and finally in cooperation with Bayne-Jones. For some years thereafter, this book did not appear on the market and was not available to the medical student, but due to the efforts of Smith and Martin and their associates, the ninth edition of Zinsser's Textbook of Bacteriology is now available.

Smith, Martin and their associates are to be complimented for their work in revising and re-editing Zinsser's Textbook of Bacteriology, which is generally accepted as a classic in this particular field. There is the added advantage that Smith, Martin, et al, not only have had the benefit of Zinsser's Textbook of Bacteriology as students, but have also had the advantage of teaching bacteriology to their own students, and have thus been able to benefit from their wide experience in bringing this book up to date.

These new authors have introduced each subject with the public health aspect of the disease. They have further added the newer investigations in the field of bacteriology and public health which accumulated during and after World War II. Since the advent of bacteriologic and cultural characteristics of organisms, emphasis has been placed in various chapters of the book so that this newer knowledge shall not escape detection by the reader. Zinsser, among other phases of his work, laid particular emphasis on immunology. The new authors have not only rewritten and brought up to date this subject within the realms of the function of their textbook, but have also rewritten the material concerning bacteriological metabolism, fungi, and virus diseases.

We can illustrate the format of this book with the subject of tuberculosis. In this chapter there is a brief resume of the public health aspects of tuberculosis, followed by discussion of the genus *Mycobacterium* found in the soil, water and air. In a clear, simple and understandable manner, there is a discussion of the cultural characteristics as well as the staining properties of the organism, tuberculin and its various products in diagnostic procedures, the effect of the antibiotics on the organism, and experimental methods for the detection of the disease. The subject is further integrated by a brief clinical resume of tuberculosis and finally the public health aspects of the subject. This method of reviewing the bacteriologic, cultural, public health and clin-

ical aspects of the disease is indeed helpful to the student. Included is a chapter dealing with technical methods of bacteriology, immunology, and serology which is ample for the medical student.

This book can be unqualifiedly recommended to the medical student and the practicing physician as a source of information in bacteriology. The publishers are to be complimented on the manner in which the book has been printed and the clear photographs that appear in the text. Although the book has been designated as a "Textbook of Bacteriology," it should be in the possession of medical students and practitioners of medicine and public health as a guide in the application of bacteriology and immunology to diagnosis, therapy, and prevention of infectious diseases.

*A Practical Manual of Diseases of the Chest* By Maurice Davidson, M.A., M.D., F.R.C.P. Third Edition, 1948. Oxford University Press.

This extensive manual, comprising six hundred and seventy pages, has been written in the best literary style and diction, and reads like a story book. The author has presented a well systematized sequence of his subject matter with appropriate illustrations and photographs of x-ray films, as well as clinical charts. He has made free use of illustrative case histories to emphasize the discussion of each subject. The more recent advances in the chemotherapy and antibiotic therapy of pneumonias have been thoroughly discussed. It has considerable material of interest to the internist, as well as the thoracic surgeon, to make the book worthy of a place in their library. Although the book is primarily written for the British public its international scope should make it one of choice for everyone interested in diseases of the chest.

#### BOOKS, REPORTS AND REPRINTS RECEIVED

*The Relationship of Tuberculosis and Silicosis* O. A. Sander, M.D., F.A.C.P.  
Milwaukee Wisconsin

*Benign Pneumoconiosis Due to Metal Fumes and Dusts* O. A. Sander, M.D., F.A.C.P.  
Milwaukee Wisconsin

*Relacoes Entre a Tuberculose Pulmonar e a Tuberculose Osteo-Articular* Lopo de Carvalho Cancellal  
Lisbon Portugal

*Micro-radiofotografia em massa resultados obtidos numa primeira observacao*  
Lopo de Carvalho Cancellal  
Lisbon Portugal

*A Posicao de Drenagem e a Penicilina Por Via Inalatoria Como Tempo Pre-operatorio da Cirurgia Pulmonar* Lopo de Carvalho Cancellal e F. Ferreira Coelho  
Lisbon Portugal

*Tratamento do Empiema Pleural Tuberculoso* Dr. Jesse Teixeira  
Rio de Janeiro Brazil

*Die primare Tuberkulose bei Erwachsenen und Kindern und ihre Entwicklung*  
Dozent Dr. Med. St. J. Leitner published by Medizinischer Verlag Hans Huber  
Bern Switzerland

*Extrapleural Pneumonolysis with Lucite Plombage* Drs. John B. Grow and Ralph E. Dwork  
Denver British Journal of Tuberculosis and Diseases of the Chest April 1948

*Colloidal Copper Morphuate* Dr. Paulo Seabra  
Rio de Janeiro Brazil



## Obituary

### PIERRE AMEUILLE

1880 - 1947

Dr Pierre Ameuille was born in 1880 in Nevers, France, and died at his home in Paris on December 19, 1947. He went to Paris to study medicine and graduated from medical school there. Dr Ameuille completed his internship at the "Hopitaux de Paris." His interests during the following period were particularly concerned with pathology and anatomic research. During the first World War, in cooperation with English medical officers, he studied many cases of war nephritis and antityphic vaccination.

Dr Ameuille was associated with the "Hopitaux de Paris" and the "Hopital Cochin" where he specialized in pulmonary diseases, tuberculosis, bronchial pathology and physio-pathology. He was President of the "Societe Medicale des Hopitaux de Paris," a member of the "Academie de Medicine," and a member of the American College of Chest Physicians, as well as a number of other societies. Just prior to his death he organized and directed the "Societe Francaise de Pathologie Respiratoire." His knowledge and intelligence, his philosophical outlook, his serenity in spite of troubles, made Dr Ameuille one of the greatest physicians in France.

J M Lemoine, M D, Paris, France

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### SIX PHYSICIANS WINNERS OF ANNUAL LIPIODOL AWARDS FOR 1948

Physicians from all sections of the country submitted examples of diagnostic roentgenography in the Annual Lipiodol Awards program for 1948. The technical excellence of the many entries offer further evidence of the great progress achieved in this specialty.

Awards were made to physicians in four categories of roentgenography. Entries submitted were judged for the extent of diagnostic features revealed and general technical excellence of plates in otolaryngology, bronchography, utero-salpingography and the delineation of sinus tracts. Physicians receiving awards were: otolaryngology, Dr Henry M Scheer, New York, bronchography, Dr J A Crellin, Philadelphia, Fellow of the American College of Chest Physicians, and Dr Lous Schneider, New York, utero-salpingography, Dr A P Echternacht, Crawfordsville, Indiana, and Dr B S Epstein, New York, sinus tracts, Dr Sidney E Foster, San Francisco, and Dr B S Epstein, New York.

Entries were reviewed by a distinguished board of judges consisting of Dr Lawrence Reynolds, President of the American Roentgen Ray Society, Dr Ira H Lockwood of Kansas City, Missouri, Dr Irving Schwartz of New York.

# DISEASES *of the* CHEST

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VOLUME XV

FEBRUARY 1949

NUMBER 2

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## Bacteriologic Examination of Tissues Surgically Removed as an Aid in the Diagnosis of Diseases of the Chest\*

HERMAN J MOERSCH M.D., F.C.C.P.,\*\* L A WEED, M.D.† and  
JOHN R McDONALD, M.D.††  
Rochester, Minnesota

With the marked progress that has been made in recent years in the treatment of certain types of pulmonary disease by means of chemical and antibiotic agents and with the advances that have been made in the successful eradication of others by means of thoracic surgery, it becomes increasingly important to determine as far as possible the underlying etiology of a pulmonary lesion so that the most satisfactory method of treatment can be employed

The importance of establishing an early and positive diagnosis in all cases of pulmonary disease is especially manifest when it is realized that carcinoma of the lung and tuberculosis have the ability to mimic practically any type of pulmonary disease. Prolonged periods of observation might often enable one to arrive at an eventual determination of the character of the lesion, but in dealing with the possibility of carcinoma and tuberculosis, time becomes a matter of greatest essence

With the improvement that has taken place in recent years in the field of thoracic surgery, it is often advisable and wise to carry out prompt exploratory thoracotomy in cases of indeterminate pulmonary disease. Such a procedure will frequently reveal unexpected and interesting findings. It is important in cases of this type, if the full value of the operation is to be attained, that

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\*Presented at the 13th Annual Meeting, American College of Chest Physicians Atlantic City, New Jersey June 8 1947

\*\*Division of Medicine, †Section on Bacteriology and ††Section on Surgical Pathology, Mayo Clinic, Rochester, Minnesota

the tissue or secretion which is removed be examined by a competent pathologist

Since time immemorial, pathologic processes have been shrouded with varying degrees of mysticism. With the development of the concept of cellular pathology and with an appreciation of physiologic mechanisms a more rational approach has been made to the understanding of disease. However, cellular pathology rests exclusively on a morphologic basis, and interpretations and opinions concerning such pathologic processes as may be observed grossly and microscopically are limited to one's ability to appreciate and recognize varying degrees of morphologic change. In the field of oncology various procedures have been developed by which one may not only recognize the nature of the tumor but may also express an opinion as to the rapidity of growth with a view to prognosticating the outcome of the disease.

With the growth of the cellular theory of pathology, technics have been developed by which the tissues to be examined are either killed by some suitable fixing agent, such as formalin or mercuric chloride, or are frozen in the fresh state so that an immediate histologic preparation may be made. The former method kills not only all the tissue cells but also the microbic agents which may be the cause of the lesion. In the second method, the handling of tissues preparatory to making the frozen section results in contamination so that a suitable bacteriologic examination may be impossible should the histologic study reveal the desirability of such examination.

Because many different infectious diseases produce histologic patterns which grossly simulate one another, it becomes the duty and the responsibility of the pathologist to be prepared to establish the nature of the etiologic agent inducing any inflammatory processes which he considers unlikely to be a part of, or related to neoplastic changes. While modern pathologists recognize the importance of consulting with bacteriologists or of making their own bacteriologic examinations, concerning certain inflammatory processes it should be emphasized that a bacteriologic examination should supplement, not replace, the histologic study, since malignant lesions may be secondarily infected and may simulate an infectious granuloma. We have found it of value to handle all thoracic surgical specimens and material for biopsy in such a manner that satisfactory bacteriologic examinations may be made in the event an inflammatory process is encountered, thus we avoid subjecting the patient to the expense and inconvenience of a repeated biopsy. The importance of such supplementary aid to the clinician and pathologist is exemplified in the following cases.

## REPORT OF CASES

*Case 1* A woman forty-two years of age who resided in Oklahoma, presented herself at the Mayo Clinic for examination on August 19, 1946. She gave a history of rheumatic pains which had been present for four years. Her primary reason for seeking medical attention at that time was to learn the nature of a questionable lesion in the pelvis.

At the time of examination the patient was found to have a small uterine fibroid. The fibroid was of such size and character that surgical intervention did not seem indicated. During the course of a general examination a roentgenologic examination of the chest revealed a discoid or globular mass lying just subcostal to the posterior portion of the tenth rib on the left side (Fig 1). This was suggestive, to the roentgenologist, of either a benign tumor or an intercostal neurofibroma. Results of examination of the sputum for acid-fast organisms were reported as negative. The urinalysis, hemoglobin determination, erythrocyte and leukocyte counts, and determination of the sedimentation rate gave values which were within normal limits, the reaction to flocculation tests for syphilis was negative.

From the history and the information at hand, it was felt that the condition might be a hamartoma although the possibility of malignancy could not be excluded. Exploratory thoracotomy seemed advisable in this case and the patient was so advised. At operation on October 29, 1946, a firm, rounded tumor mass was found situated near the periphery of the lower lobe of the left lung. This mass was excised. The specimen removed was reported by the pathologist as having the gross and microscopic appearance suggestive of healed primary tuberculosis (Fig 2). Material from the tumor mass was injected into guinea pigs in order to determine definitely the underlying etiologic agent. Much to our surprise, when the animals were examined at necropsy eight weeks later they were found to be infected with *Coccidioides immitis* and there was no evidence of tuberculosis. Because of this report, the original tissue was re-examined and additional sections were taken from the tumor mass, at this time numerous small spherical bodies were recognized. Some of these bodies appeared to be in the budding form, but none could



FIGURE 1

*Fig 1 (case 1)* Circumscribed tumor mass in left base



FIGURE 2

*Fig 2 (case 1)* Gross appearance of tumor removed

be found which had the endosporulating spherules characteristic of coccidioidomycosis

In retrospect, the diagnosis of this lesion might have been made if a skin test for coccidioidomycosis had been carried out. However, the clinical history and the fact that the patient came from a part of the country where coccidioidomycosis is not endemic did not arouse our suspicion of a coccidioidomycotic infection. The case does emphasize the importance of keeping the possibility of coccidioidomycosis in mind in all cases of pulmonary infiltration. Although surgical intervention is not recommended as a routine procedure in coccidioidomycosis, it is of interest that this patient made very satisfactory progress after the removal of the coccidioidal nodule from her lung. It is, of course, problematic whether the improvement in her general rheumatic pains can be justifiably ascribed to the removal of this nodule.

*Case 2* A woman forty-six years of age who came from Minnesota was admitted to the clinic September 18, 1946. Her chief complaint was that of cough and expectoration. She stated that her difficulty began after an attack of pneumonia in 1919. Since that time she had suffered from a chronic cough and had been subject to frequent pulmonary infections. For the past five years she had coughed up a great deal of purulent secretion, the quantity varied from a half teaspoonful to a half cupful in twenty-four hours. After overexertion the sputum had at times been blood streaked. During the past year the patient had noted an increasing degree of dyspnea associated with exertion.

On physical examination the only essential findings were a slight



FIGURE 3

*Fig 3 (case 2)* Contraction of right lower lobe



FIGURE 4

*Fig 4 (case 2)* Bronchiectasis of right lower and middle lobes

limitation in movement of the right side of the chest on respiration and a few coarse rales heard over the right lower and middle lobes. When the patient was tipped over she expectorated a characteristic bronchiectatic type of sputum. Roentgenologic examination of the chest was reported as showing probable contraction of the right lower lobe (Fig 3). Sputum examination did not reveal acid-fast organisms. Bronchoscopic examination was performed and a large amount of purulent secretion was found coming from the bronchi of the right lower and middle lobes. The mucous membrane of the bronchus of the right lower lobe was markedly inflamed. No evidence of a tumor or stenosis of the bronchus was seen. Bronchograms were made the following day, these showed evidence of bronchiectasis involving the right lower and middle lobes (Fig 4).

A diagnosis of bronchiectasis involving the right lower and middle lobes was made and operation was advised. After preoperative nebulization with penicillin the patient was operated on on October 26, 1946. The middle lobe was found to be completely atelectatic. A right middle and lower lobe lobectomy was performed. On gross and microscopic examination the pulmonary tissue removed showed the characteristic appearance of bronchiectasis with associated pneumonitis (Fig 5a). Since pneumonitis is a common finding in bronchiectasis, in this case it was not thought necessary to carry out further pathologic or bacteriologic studies to determine the etiology of this lesion.

After the operation collapse of the right upper lobe developed. In spite of repeated bronchoscopic aspirations the right upper lobe failed to re-expand. It became necessary to perform a right upper lobe lobectomy in December 1946. The gross and microscopic appearance of the right upper lobe was the same as that found in the right lower and middle lobes at the time of their removal, except that the degree of bronchiectasis was less marked (Fig 5b). The material removed at this time was subjected to bacteriologic examination and was found to contain *Pasteurella* of the animal variety *Empyema* of the right side of the chest developed after the right upper lobe lobectomy, drainage was obtained by open operation. Although the *Pasteurella* in this case was found to be resistant to streptomycin *in vitro* the antibiotic agent was instilled into the empyema pocket with apparent benefit.

There might be some question as to whether the *Pasteurella* infection in this case was primary or secondary in nature. In any case, it is unusual that the involvement of the upper lobe should have occurred after the lower and middle lobe lobectomy and that the pathologic process found in all three lobes was identical in nature. It would seem that the *Pasteurella* was the underlying etiologic factor in this case.

*Case 3* A man thirty-two years of age whose home was in Mexico came under our care on September 26, 1946 stating he had cancer of the lung. He said that he had enjoyed good health until May 1946, when he first noticed a sharp pain in the left side of the chest. The pain was not related to respiration and lasted but three days. With the onset of the chest pain he noted an elevation of temperature to 40.5° C. Roentgenologic examination of his chest at that time was reported as disclosing evidence of an area of infiltration which involved the left lower lobe.



FIGURE 5 (case 2) (a) Section of right lower lobe ( $\times 3$ )  
(b) Section of right upper lobe ( $\times 35$ )

and which led to a diagnosis of congestion of the left lower lobe. The patient was treated with injections of penicillin without apparent improvement. His temperature remained elevated for twenty-one days. Since the onset of illness the patient had lost weight. He had had a very slight, unproductive cough. Because the roentgenograms of the chest failed to show evidence of any improvement, carcinoma of the lung was suspected and the patient was referred to us for treatment.

The patient was found to be a well-developed, healthy-appearing man with normal blood pressure, pulse and temperature. Physical examination of the chest gave essentially negative results. Urinalysis, hemoglobin determination, erythrocyte and leukocyte counts and differential count gave results which were within normal limits and the reaction to the flocculation test for syphilis was negative. It was impossible to obtain sputum for culture or microscopic examination for tuberculosis or for examination for malignant cells. A roentgenogram of the chest made on September 27, 1946, showed evidence of a lesion in the left lower pulmonary field which was partially obscured by the left side of the heart (Fig 6). The lesion was considered by the roentgenologist to be probably a hamartoma. Bronchoscopy was done and gave entirely negative results. The history of pulmonary difficulty of four months' duration, with loss of weight and a persistent nonresolving chest lesion as seen on roentgenologic examination, made the diagnosis of carcinoma very probable.

Exploratory thoracotomy was advised. The patient was operated on on October 26, 1946, and a lesion was found situated in the inferior portion of the left upper lobe which appeared to be inflammatory in nature. It was adherent to the pericardium as well as to the chest wall. A left upper lobe lobectomy was performed. The specimen removed was reported by the pathologist as being a granulomatous inflammatory mass, possibly a lesion of coccidioidomycosis (Fig 7). However, no endospore-forming spherules were found although budding forms were present, suggesting the possibility of blastomycosis. Bacteriologic studies of the tissue revealed large numbers of *Coccidioides immitis*, no blastomycetes were recovered in the culture, although their presence had been sug-

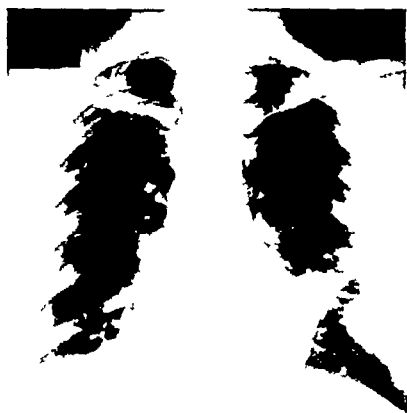


FIGURE 6

Fig 6 (case 3) Lesion in left lower pulmonary field



FIGURE 7

Fig 7 (case 3) Mass removed at operation



gested by the appearance of the budding forms in the microscopic examination. Coccioidin skin tests were done after operation, and the results were found to be positive.

In this case, the possibility of coccidioidomycosis should undoubtedly have been suspected before operation, however, this disease was not suspected and it was necessary for the bacteriologist to have special studies carried out in order to permit determination of the exact cause of the patient's difficulty. This patient did very well after operation.

*Case 4* A woman forty-nine years of age came to the clinic for examination on March 3, 1947. She had always enjoyed good health until February 19, 1946. At that time she suffered from a sore throat which she stated was not severe and which lasted but a few days. Four days later a red rash developed on the left shin, followed in a few days by similar lesions on both wrists and hands. The patient described these lesions as looking like burns. The onset of the skin lesions was associated with an elevation of temperature to 102° F. The patient was hospitalized in her home community for three weeks, during which time the skin lesions disappeared and the temperature returned to normal. At the end of her period of hospitalization, her abdomen began to enlarge and she suffered from increasing dyspnea on exertion, orthopnea and severe edema of the lower extremities. She was again hospitalized and kept in an oxygen tent for seven weeks. She stated that during this period she had generalized edema with daily fever, periods of delirium and a pleural



FIGURE 3 (case 4) Encapsulated empyema and thickening of pleura

effusion on the right side. Aspiration was performed two times and both times the fluid removed was reported as clear. By June 1, 1946 most of the afore-mentioned symptoms had subsided. On December 10, 1946 she again suffered from a sore throat with elevation of temperature to 103° F, a cough and expectoration of small amounts of yellowish sputum, hemoptysis did not occur. The cough persisted for one week and then disappeared. However, a low-grade fever persisted until February 19, 1947. During this entire episode the patient lost forty-five pounds (20.4 kg).

At the time of our examination on March 3, 1947 the patient was very thin, weighing but a hundred pounds (45.4 kg), she obviously was ill. On physical examination the right side of the chest was found to be retracted, with lagging of this side on respiration, there was dullness to flatness to percussion over this side with diminution of breath sounds. Roentgenographic examination of the chest was reported as revealing an encapsulated empyema on the right side with rather marked thickening of the pleura, a fluid level was present opposite the seventh interspace posteriorly (Fig. 8). Urinalysis, hemoglobin determination, erythrocyte and leukocyte counts and differential count all gave results which were within normal limits. Blood smears showed no significant changes. The sedimentation rate was 70 mm in one hour (Westergren). Examination of the sputum for acid-fast organisms gave negative results.

A diagnosis of empyema of the right side of the chest was made and



FIGURE 9 (case 4) Direct smear of tissue showing sulfur granules ( $\times 720$ )

a diagnostic aspiration was carried out on March 5, 1947, when 50 cc of thick greenish gray purulent material was aspirated. This material was examined for acid-fast organisms and for sulfur bodies with negative results. The patient was operated on on March 7, 1947, the surgeon carrying out resection of four ribs with decortication of the right lung for chronic empyema. Multiple bronchial fistulas were noted at the time of operation. A moderate amount of pus was found in the pleural cavity, this material contained multiple small, yellowish sulfur bodies which the surgeon considered to be diagnostic of *Actinomyces*. Careful bacteriologic studies of the granules, however, showed them to be composed entirely of large, branching filaments which were finally identified as *Aspergillus fumigatus* (Fig 9). Results of studies on guinea pigs were negative for tuberculosis. No other microbic agent was ever obtained in cultures taken from the empyema cavity and it was therefore concluded that the pulmonary lesion was that of aspergillosis. The patient was treated with large doses of penicillin after drainage of the empyema cavity, she showed marked improvement in general health.

**Case 5** A man thirty-four years of age who resided in southern California, first came under our observation on September 25, 1946. A month before admission he had first suffered from a dull headache associated with soreness in the back of the neck. He also noted some pain in the right upper part of the chest on deep respiration. He became apprehensive that his condition might be due to poliomyelitis, as there were a number of cases of this disease in his neighborhood at the time. A roentgenogram of the chest made by his family physician showed evidence of a lesion in the right lower lobe. He was found to have a temperature of 100° F. He was placed in the hospital and penicillin was started along with sulfadiazine. The sulfadiazine was soon discontinued because of the development of a generalized rash. At the end of a week the patient felt considerably better but the pain in the chest persisted.

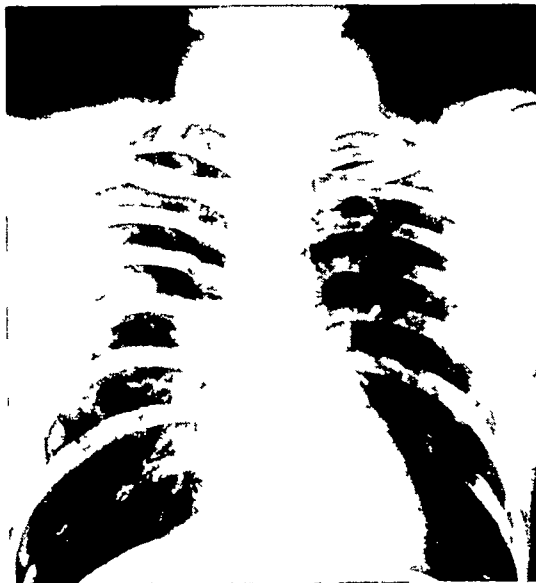


FIGURE 10 (case 5) Lesion in right lung at level of third rib anteriorly. Note cavity

During the period of hospitalization eight examinations of sputum were carried out and all were reported negative for tubercle bacilli. As the chest lesion seen on roentgenologic examination persisted, a diagnosis of carcinoma was suspected and the patient was referred to the clinic for further study.

At the time of admission to the clinic the patient's only complaint was that of pain in the thoracic part of the spinal column. The patient was a well-appearing, well-developed young man. Physical examination of the chest failed to reveal anything of diagnostic importance. On palpation of the neck a hard gland was found in the right supraclavicular region. The roentgenogram of the chest showed a lesion to be present in the right lung at the level of the third rib anteriorly, with associated fibrosis extending to the second interspace anteriorly (Fig 10). It was felt that the possibility of tuberculosis must be considered. The sedimentation rate was 53 mm in one hour (Westergren). Examination of the sputum did not reveal acid-fast organisms. Other laboratory tests were all found to give essentially negative results.

From the history it was believed that the patient's pulmonary lesion was probably on an inflammatory basis and the possibility of a tuberculous infection was strongly entertained. The supraclavicular lymph node was removed for biopsy and on microscopic examination revealed, both in the fresh frozen and the fixed sections, the histologic picture

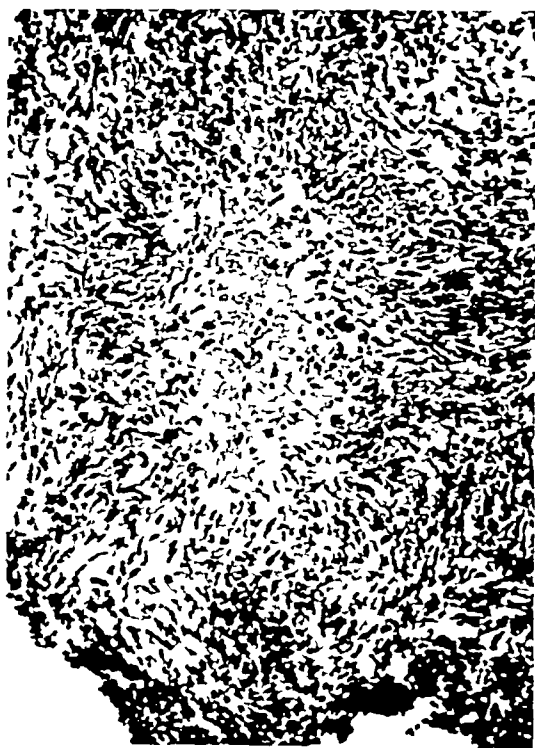


FIGURE 11 (case 5) Section of supraclavicular lymph node. Histologic picture is that of tuberculosis (x160).

of tuberculosis (Fig 11) Stains of the tissue for acid-fast organisms failed to reveal the presence of any such organisms In guinea pigs inoculated with material from the lymph node, lesions developed which were suggestive of tuberculosis at the time the lesions were examined at necropsy eight weeks after inoculation Further studies of the tissue, however, showed no acid-fast organisms to be present, but there were many endosporulating spherules characteristic of *Coccidioides immitis* (Fig 12) This was proved to be the etiologic agent by additional cultures and animal studies

Here again we have striking evidence of the importance and value of bacteriologic study of tissue which, on microscopic examination, is not entirely diagnostic It emphasizes the importance of close co-operation between the pathologist and the bacteriologist Perhaps in this case the possibility of coccidioidomycosis should have been suspected as the patient came from California

*Case 6* A young man twenty-three years of age had always enjoyed good health until three years before coming under our observation, at the onset of illness he first had started to lose weight and to fatigue easily He felt especially exhausted at the end of a hard day's work During the next four months he lost fifty pounds (22.7 kg) and it was necessary for him to retire from his work and to remain at rest Two

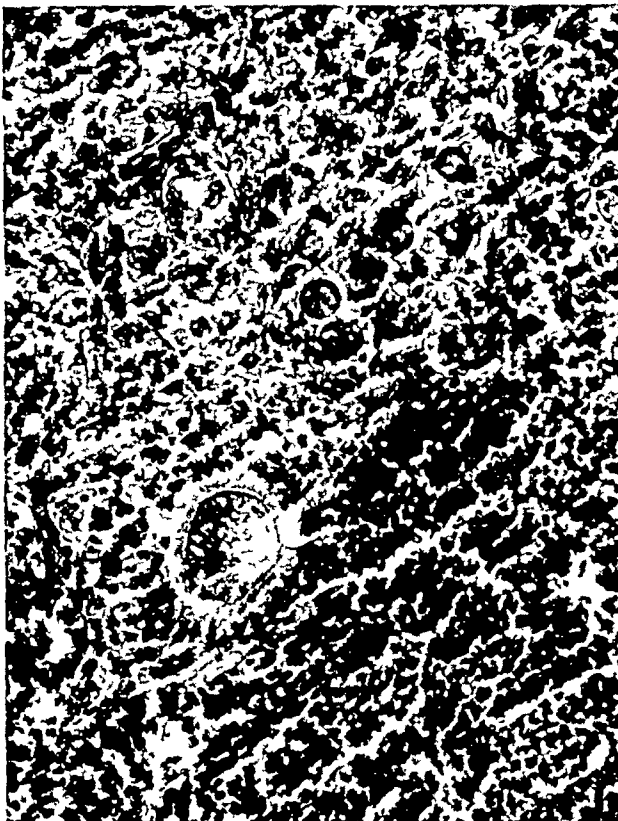


FIGURE 12 Endosporulating spherules characteristic of *Coccidioides immitis* ( $\times 255$ )

months later he experienced profuse night sweats for several weeks and began to run a low-grade fever. A year after the onset of his difficulty he had seemed to improve and again had returned to work. A month after his return to work a sore spot in the pharynx and swollen, tender, bleeding gums developed. This was diagnosed as trench mouth for which he received treatment without much success. A roentgenogram of the chest was made at the time that the sore mouth developed, and this was reported as showing a clouding of the central portions of both lungs, a diagnosis of tuberculosis was suspected. He was sent to a tuberculosis sanatorium, where he remained for three months. At the end of that time he was discharged because they were unable to confirm the diagnosis of tuberculosis. During the next year the patient remained at rest but still continued to feel fatigued, weak and short of breath on exertion, and had a sore mouth.

At the time of our examination the patient was found to be an undernourished young man who was obviously ill. It was noted that he had several raw areas on the right side of the throat and in the back of the mouth. The gums were swollen and boggy and tended to bleed on manipulation. The remainder of the physical examination revealed nothing of diagnostic importance. Roentgenographic examination of the chest disclosed an extensive pulmonary fibrosis which was much more marked in the middle third of both lungs, with compensatory emphysema in the bases and apices. The roentgenologist thought that the possibility of a fungus infection or sarcoidosis should be excluded (Fig 13). Examination of the sputum for acid-fast bacilli gave negative results. The sedimentation rate was 65 mm. in one hour (Westergren). The reaction to the tuberculin test was reported as negative. Special laryngologic exam-



FIGURE 13 (case 6) Marked pulmonary fibrosis and compensatory emphysema

ination revealed a granulomatous lesion 1.5 cm in diameter on the right side of the soft palate near its posterior border. There was another lesion of about the same size a little farther forward near the junction of the hard and soft palates on the right side. Another was seen in the left lower alveolobuccal fold opposite the cuspid region, and a fourth involved almost the entire left side of the floor of the mouth. There was also a small lesion involving the right tip of the epiglottis. A specimen was removed from these lesions for biopsy which on microscopic examination was reported as showing evidence of tuberculosis. However, acid-fast organisms could not be demonstrated in the lesions and guinea pigs inoculated with the material failed to show evidence of tuberculosis. Special bacteriologic studies however revealed the presence of *Histoplasma capsulatum* (Fig 14).

### SUMMARY

Obviously, it should be our cherished goal to try to establish a positive clinical diagnosis in every case of pulmonary disease. Careful and diligent use must be made of the many useful tests and examinations that are available for this purpose. The close co-operation of the roentgenologist, bronchoscopist, bacteriologist and other specialists is highly important. Despite all this, there will remain a goodly number of patients suffering from pulmonary disease in whom a positive diagnosis cannot be arrived at. It is often unwise, in a case of this type, to procrastinate too long with periods of observation or with tests that require many weeks for completion, because of the danger that the lesion may be malignant in nature, thereby requiring prompt treatment if it is

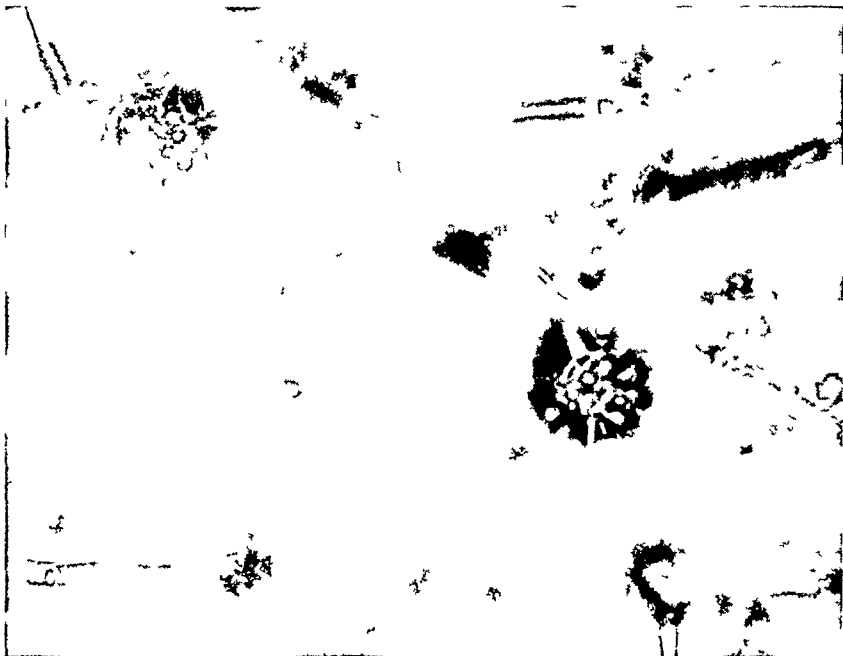


FIGURE 14 (case 6) *Histoplasma capsulatum* (x950)

to be eradicated successfully In properly selected cases of this type, exploratory thoracotomy is often indicated, the pathologist can often furnish a prompt explanation of the underlying cause of the pulmonary lesion In cases in which the cause is uncertain, bacteriologic studies of the tissue should be employed, as often useful information which might otherwise escape detection may be obtained by this method

### RESUMEN

Naturalmente que nuestro propósito debe ser el tratar de establecer un diagnostico clinico positivo en todo caso de enfermedad pulmonar Se deben emplear con cuidado y diligencia las muchas pruebas y exámenes valiosos disponibles para este proposito La íntima cooperación entre el roentgenologo, broncoscopista, bacteriologo y otros especialistas es sumamente importante A pesar de todo esto, quedara un numero crecido de pacientes que padecen enfermedades pulmonares en los que no se puede hacer un diagnostico positivo En casos de este tipo, a menudo no es prudente dilatar por mucho tiempo con periodos de observación o con pruebas que requieren muchas semanas para completarse, debido al peligro de que la lesion sea de naturaleza maligna y que, por consiguiente, exiga pronto tratamiento para erradicarla con buen éxito En casos de este tipo, propiamente seleccionados, se indica frecuentemente la toracotomia exploratoria, pues a menudo el patologo puede suministrar una pronta explicacion de la causa de la lesion pulmonar En casos en los que la causa es incierta deben emplearse estudios bacteriologicos del tejido, pues mediante este método con frecuencia se puede obtener informacion util que de otra manera podría pasarse por alto

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### D I S C U S S I O N

HOLLIS E JOHNSON, M.D., F C C P  
Nashville, Tennessee

We are indebted to Dr Moersch for bringing us the experience of his group in handling pathologic specimens so that they may also be studied bacteriologically This presentation is timely for two reasons, first, because coccidioidomycosis is being encountered by some of us who had only read or heard of it before the war This is due to the fact that many of our soldiers were trained in areas where the disease is endemic Second, because the work of Drs Christie and Peterson has added Histoplasmosis to the list of diseases we must differentiate from tuberculosis



Diseases of the chest are of such complex forms that it is necessary to have the services of many people in order to make a satisfactory diagnosis, and it goes without saying that the various ones concerned must conduct their examinations in such a way as to be of all possible help to each of their colleagues in their part of the examination

It has been our custom for several years to examine granulomatous and ulcerative tissue obtained by bronchoscopic biopsy both histologically and bacteriologically. Such examinations are not routine but have been of distinct value in several cases.

We also have studied lymph glands obtained by biopsy, both bacteriologically and pathologically, when the differentiation between tuberculosis, Boecks sarcoid, cancer, and Hodgkins disease was to be made. The material so obtained has been sectioned and studied for tubercle bacilli as well as abnormal cells, and at the same time has been inoculated into guinea pigs and cultured.

This method of study resulted in some unexpected diagnoses of Histoplasmosis and coccidioidomycosis and has been helpful in establishing diagnoses of undulant fever.

More recently, in connection with his study of histoplasmosis, Dr. Amos Christie has added an expert mycologist to his staff, and I am privileged to report briefly some of their cases which will be reported in detail by them later.

In one case, a diagnosis of Hodgkins disease had been made by biopsy ten years previously. The patient continued to have the enlarged cervical lymph glands but was little if any worse. Biopsy and histological and bacteriological examination revealed *Histoplasma Capsulatum*. A second case was that of a young white woman who had an acute infection of her cervical lymph glands which yielded to penicillin but relapsed while under treatment. A biopsy of one of the cervical glands revealed the yeast cells of *Histoplasma Capsulatum*.

Recently a series of 75 cases of unidentified granulomatous material obtained at autopsy was studied bacteriologically, and four of them yielded definite *Histoplasma Capsulatum* and four have been tentatively identified as the same organism.

Another case, a child that died of dysentery just before I left Nashville, was autopsied and material obtained from the intestines was cultured on culture media to which penicillin and streptomycin had been added. A pure culture of *Histoplasma Capsulatum* was obtained.

This experience is testimony of the value of cooperation between the clinician and the pathologist and the bacteriologist.

Dr. Moersch and his group have brought us a timely and stimulating report of excellent work.

## D I S C U S S I O N

SEYMOUR M. FARBER, M.D., F.C.C.P.

San Francisco, California

Drs. Moersch, Weed and McDonald again have emphasized the value of bacteriologic studies of surgical specimens. Of particular interest to me were the three cases of coccidioidomycosis which illustrated how bacteriologic studies of a surgical specimen will alter a diagnosis. At the University of California we have recently reviewed 31 patients with coccidioidal infections. Seven of these patients entered with a provisional diagnosis of coccidioidomycosis. The remaining patients entered with varied diagnoses such as arthritis, chronic sinusitis, bronchitis, bone abscess, sarcoma of the ileum, malignancy of the skin, etc. By means of bacteriological studies a definite diagnosis of coccidioidal infection was established in 11 of these patients. Four of the others had biopsies but unfortunately cultures were not taken.

With the increasing number of cases of coccidioidomycosis being reported in various parts of the United States it is important that clinicians emphasize bacteriologic studies of surgical specimens. The six cases reported by the authors splendidly illustrate the need of these studies.

# An Appraisal of the Results of a Six-Year Tuberculin and Mass X-Ray Survey of the Population of Asuncion: Based on More Than 100,000 Tests\*

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and J A CORONEL VERA, M D  
Asuncion, Paraguay

## *Introduction*

We can say that up to the last ten years the prophylaxis against contagious diseases was in the hands of Dispensaries whose task was reduced to the medical examination and treatment of all persons who came to the Dispensaries with likely symptoms of disease and very rarely as a preventive measure against disease. The only epidemiological basis on which prophylaxis rested was that of the above-mentioned means and compulsory reporting of disease. Under such conditions tuberculosis prophylaxis was well nigh illusory inasmuch as the only diseased persons examined were those who presented themselves at our only Dispensary. As for the compulsory declaration of disease the results obtained were very far below the real state of affairs in our case and it is also among other communities.

Diseased persons who were apparently healthy were never examined. Those suffering from contagious diseases (tuberculosis, syphilis, leprosy, etc.) entered every profession and took part in public activities although they were a constant source of danger as carriers of such diseases. It was absolutely essential to face the problem by examining everybody, whatever their occupation and station of life.

With the object of controlling the state of health of the general public and to take measures tending to improve and maintain it at a satisfactory level, a government decree, in October 1936, made the Health Card compulsory for all persons engaged in the manufacture and sale of food-stuffs and merchandise. In September 1938 this law was amplified to include all public servants, workmen, clerks, students, teachers, domestic servants, etc.

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\*Report on the Prophylaxis and Epidemiology of the Tuberculosis Department, Asuncion, Paraguay (Health Control Institute for Individuals and Communities, Director Dr A R Gines, Profesor of Internal Pathology) Presented on the International Night Program, Thirteenth Annual Meeting, American College of Chest Physicians, Atlantic City, New Jersey, June 5, 1947

Nevertheless, it was necessary to exercise special control over the chest diseases, which accounted for 50 per cent of the deaths in Asuncion in 1941 (pulmonary tuberculosis, pneumopathies and heart diseases, respectively)

The Government assigned us the task of setting up the Organization and Administration of the Prophylaxis and Epidemiology Section of Tuberculosis in July 1941, and the results demonstrated the importance of the x-ray-tuberculin survey among the more important nuclei of the Capital (asylums, the Military School, Municipality, National Printing Office, textile factories, the interned and the staff of the reformatory for females, employees and attendants of the Clinical Hospital, and the relatives of persons suffering from tuberculosis)

Based on results obtained through our previous work the possibility of carrying out a mass x-ray and tuberculin survey in the city was favorably received and a decree issued in November 1941 widened the scope of the previous one thereby ordering the inclusion of the x-ray photograph as a compulsory prerequisite for securing the Health Card in Asuncion

The voluntary, private and collective medical examination was thereby complemented by the compulsory examination of all persons in active employment in our midst. As a matter of fact, voluntary examinations (which we still continue to perform without charge, and to which we give wide publicity on the radio and in the newspapers) have proved inadequate in obtaining good results. We are of the opinion that the same state of affairs will be found to exist in the majority of South American cities. As a consequence of this, and as an essential medium for getting satisfactory results, we recommend compulsory Health Cards which may be only issued after an x-ray and tuberculin examination has been made by a competent organization, such as our own Institute of Control of the Health of Persons and Communities, at least, in the case of populous cities.

It is understood that case finding can be conducted in two special ways which complement each other. One way is the "prophylaxis of the source" which is also called "centrifugal prophylaxis" the object of which is to discover new cases among those persons who are in contact with the patient. The second way is to carry out the preventive examination of all persons in the community without taking into account possible contacts. Mass x-ray examination of the community achieves this objective. It is by these means that we also carry out "centripetal prophylaxis" which discovers hitherto unknown sources of the disease among the apparently healthy. The periodical repetition of the examina-

tion will show lower figures for diseased persons owing to the constant control of the detected sources (See Fig 1)

When we took charge in June 1941 of the organization and administration of Prophylaxis and Epidemiology of Tuberculosis in this country we adopted as a basis the above-mentioned method and, among other measures taken by us, such as the prophylaxis of the sources of the disease, sanitary education, BCG vaccination, requests for the construction of sanatoria and hospitals, and the setting up of Social Insurance for people suffering from tuberculosis, we adopted in an ample fashion the system of the examination of communities in Asunción. In order to carry out the task before us we resorted to the compulsory Health Card system and the possession of which calls for periodic roentgen-photographic examination and tuberculin tests as well as other examinations whenever necessary.

By these means we have filed about 130,000 micra roentgen-photographs which correspond to 75-80,000 persons who were examined by us out of a total population of 126,000 according to the last census (1946)

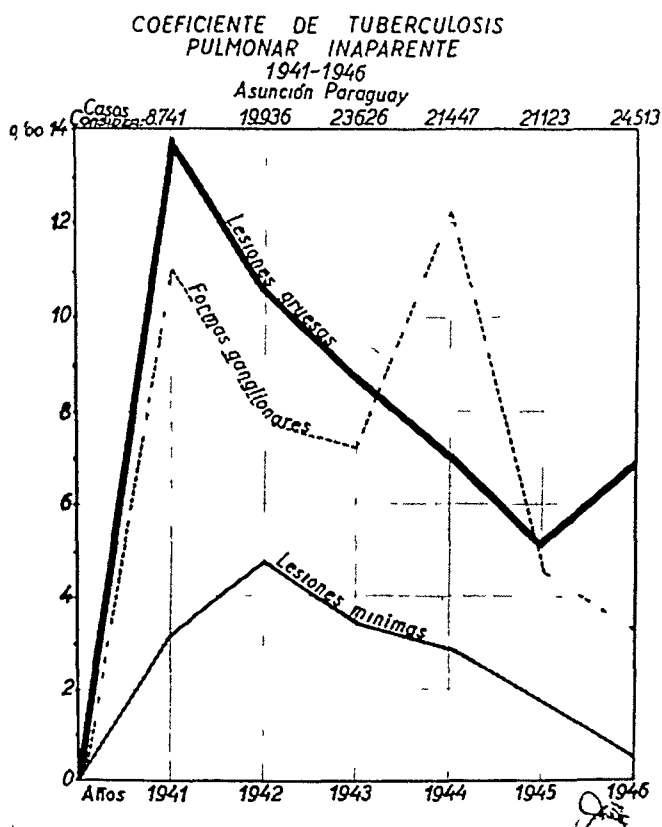


FIGURE 1

### *Diagnosis Technique*

We include in our diagnostic technique the following

- a) Tuberculin test
- b) Abreu's roentgenphotograph or microfilm
- c) Standard x-ray picture (30 x 40 cm )
- d) Laboratory work including analysis of sputum, blood sedimentation rate and occasionally a haematological examination. Studies of the gastric contents are rarely carried out. Instead we have introduced bronchial washings (methods of Abreu and R. Fernandez)

a) *Tuberculin test* In 1941 we carried out von Pirquet's test and from 1942 we used the intracutaneous test (Mantoux) with tuberculin solution 1/1000 as first test. Vollmer's patch was only used as an experiment. The second test, for non-reactors, was carried out directly with tuberculin 1/20. The tuberculin used in all these tests is that of synthetic medium (SOT) made by the Instituto de Higiene de Montevideo.

b) *Abreu's X-ray photography* Roentgenphotography is, without any doubt whatsoever, the axis on which the new style prophylaxis of tuberculosis revolves. While x-ray pictures would certainly be the ideal method, we are faced with the decided handicap of the price of the film which makes its use prohibitive in the examination of communities.

The film we use is Kodak Super XX which gives thirty-six exposures. The technique employed is as follows: 60 milliamperes and variable kilovoltage, according to the ventrodorsal diameter of the person examined, which runs from 50 to 80 Ky. The exposure time ranges from 5/10 to 9/10 of a second and very occasionally 1.5 seconds.

The rolls of film are then studied with the aid of a magnifying glass. It should be said that the diagnosis obtained by this method are almost never exact. They just serve as a means of selection. As a consequence all lung shadows, mediastinum or otherwise of the chest, must be checked first of all by means of an x-ray picture in order to reach an exact diagnostic conclusion as to the existence and the type of lesion discovered.

Potter's system, or rather roentgenphotography on 10 x 12 cm films used in the United States, especially after its introduction in 1938 by Potter in collaboration with the General Electric X-ray Corp., has now been put into operation effective May 1947.

### *Examination Procedure*

This is based mainly on the Health Card system, but we also examine people who solicit such an examination, and we carry

out examination of those persons sent to us by private practitioners or school doctors. In this way it may be said that we have examined practically everybody in every trade, whatever their sex or age.

The examination is the same in every case. Employees and professional workers are required to pay a fee of 3.00 pesos (\$1.00) for Health Card while other persons are examined free of charge.

By methodical work we are able to take one x-ray photograph every minute, which gives us a total of 60 per hour. The procedure is best described as follows: (a) Presentation of the person to be examined in the Tax Office where he pays his fee. (b) Details and indexing. (c) Tuberculin test. (d) Micro-roentgen photograph. The result of each examination is made known within 48 hours. In doubtful cases an x-ray photograph is requested and when negative reactors appear we use the second Mantoux test with 5 milligrams of tuberculin. If the x-ray picture examination confirms our suspicions we carry out examinations of the sputum and blood sedimentation rate. (See Plan).

The patient is then sent, along with the respective communication, to the Dispensary, or the Tuberculosis Hospital or to a private physician.

If the second tuberculin reaction is negative and the x-ray photograph is normal we carry out vaccination with BCG (Rosenthal method).

On the Health Card which we issue to healthy persons we write down the number of examinations of the holder and the pertinent remarks relative to periodical examination, BCG vaccination, etc.

The results of the different examinations are filed in special cabinets in numerical and alphabetical order, and also in books destined for special remarks on each type of examination. The standard x-ray pictures are also filed in the same fashion.

Those persons found to be suffering from disease are reported to the Department of Hygiene every month. These monthly lists, along with the names sent in by other branches are filed in alphabetical order and also according to the individual's trade or occupation.

People with aortic and heart diseases are notified by means of their respective Health Cards to have a further and final clinical examination in a hospital or by a private physician.

We take an x-ray photograph (35 mm) every two years of a normal person. The Health Card must be renewed every year and on these occasions we make a complete examination of the skin in order to detect syphilis and other contagious diseases.

The procedure of the community examination used in Asunción since the year 1941 is shown in the "Working Plan" Chart.

*Working Plan of the Health Control Institute for  
Individuals and Communities*

VOLUNTARY EXAMINATION (free of charge)	COMPULSORY EXAMINATION
CARD RECORD TUBERCULIN TEST X-RAY PHOTOGRAPH	TAX OFFICE Tax Gs 3 00 (\$1 00)
	RENEWAL of HEALTH CARD CHECK ON PREVIOUS YEAR'S HEALTH CARD SKIN EXAMINATION
FINAL RESULTS (48 hours later) Normal HEALTH CARD or TICKET (free Health Card)	PENDING RESULTS of
	OTHER EXAMINATIONS Standard Tuberculin Test Standard X-Ray Picture Cardiovascular control Laboratory examination
FINAL RESULTS	
Normal Non-reactor B C G Vaccination HEALTH CARD or TICKET (free Health Card)	Patient HOSPITALS DISPENSARIES PRIVATE PHYSICIANS SOCIAL INSURANCE

*Epidemiological Data*

Before we summarize the results obtained it should be mentioned that in Asuncion the actual tuberculosis mortality is 20 per 10,000. The infection index as revealed by tuberculin tests varies from 91 to 97 per cent for the population taken as a whole and shows very high figures for the first years of life 50-60 per cent from 0 to 5 years, 70-80 per cent from 6 to 10 years, and 80-90 per cent at the age of 15. Latent morbidity was 2-3 per cent during 1941 and 1942 and showed 6-20 per cent chest lymph node tuberculosis in children under the age of six and 4-10 per cent for those 6 to 10 years of age.

These figures demonstrate the period of massive tuberculosis through which we are passing. The epidemic curve, as judged by the tuberculosis mortality index compiled since 1895, must have commenced during the last century since very high percentages, almost comparable to those of the present, have been registered since the beginning of the present century. The lack of statistical data does not permit further information.



### Results

Owing to the extent which a full description would demand we shall limit ourselves to a summary of the full report presented before the Seventh Pan-American Congress of Tuberculosis (Lima, Peru, January 1947)

The results and conclusions arising from the study of 105,898 persons who underwent the tuberculin tests (repeated on non-reactors up to 5 milligrams Mantoux), 119,386 x-ray photographs, 5,000 roentgenograms of different chests (30 x 40 cm) and some laboratory work on sputum and blood sedimentation rate, are complemented by the prognostic study of the different kinds of lesions found during our investigations, and also that of apparently normal people without radiological evidence of pulmonary lesions who some time after become ill or die from tuberculosis

A) *Tuberculin and roentgenphotography test results* can be divided in a) Epidemiological and b) Clinical

#### a) *Epidemiological contribution*

1) The high annual positive tuberculin index (91-97 per cent) for all ages, 50-60 per cent for the first five years of life, 60-80 per cent for children 6-10 years of age and as high as 95 per cent around 20 years of age, the high index of latent morbidity appraised for the lymph node form is 6-20 per cent for the first five years of life, 4-11 per cent from 6-10 years of age, and 1-2 per cent up to the age of 15, to which must be added the minimal lesions in a proportion of rather less than 1 per cent, and gross lesions whose proportion varies between 1-2 per cent from 16 to 50 years of age and which is subject to a considerable increase after the age of fifty which brings about a percentage of 3-4, go to show that the city is going through a period of massive infection, which is in accord with its high ratio of tuberculosis mortality (about 20 in 10,000)

Among the *lymph node* forms we include hilar, mediastinal and tracheobronchial lymph nodes, some of them with infiltrative pulmonary lesions all of which can be styled as "infantile forms" or "primary infection" Among the *minimal lesions* we include nodules, local thickness of the broncho-vascular tissue with exudative aspects, fuzzy at the edges, excluding the hard tissues and nodules *Gross lesions* include all those forms known as "reinfection" whatever their type (exudative, proliferative, mixed or destructive) and whatever the extent, be it infiltrative or phthisic, in other words, a large part of the minimal and all the moderately advanced and far advanced forms according to the North American

classification The active pleural forms are classified in this group while the residual lesions are excluded

2) The mass x-ray examination, or the search for tuberculosis among the apparently healthy, has brought about a progressive annual decline in the infection index (including the hyperergics) and of the latent morbidity index in its adenopathic forms, both minimal and gross These reductions, which correspond to all ages, although more pronounced among those of tender age, taken as a whole show the following figures for 1941, 1942, 1943, 1944, 1945 and 1946 respectively (See Fig 2)

b) *Clinical contribution* A clinic-radiological appraisal of the different tuberculin allergy based on 2,000 reactors in each group reveals

1) The negative reaction allows us practically to exclude latent active tuberculosis We have to make an exception of healthy normergics (nonreactors) under the age of 20 in whom we have found 0.15 per cent of tracheobronchial lymph nodes and 0.50 per cent of hilar lymph nodes of supposed bacillary etiology which would be found during the so-called pre-allergic period, and 0.10 per cent of infiltrative processes whose bacillary etiology could not be determined The presence of calcifications in persons from

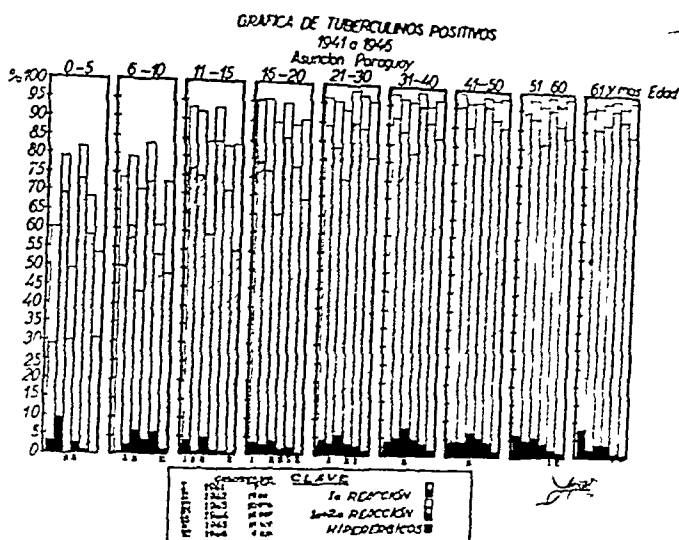


FIGURE 2

Allergic curve 96.4 95.8 91.3 96.9 93.8 and 93.9 per cent  
 Hyperergic curve 4.2, 3.5 5.3 3.4 2.1 and 1.1 per cent  
 Adenopathic forms 1.11 0.78 0.72 1.21 0.44 and 0.37 per cent  
 Minimal lesions 0.32, 0.48 0.34 0.29 0.17 and 0.05 per cent  
 Gross lesions 1.38 0.06 0.87 0.70, 0.51 and 0.68 per cent

2 to 60 years of age in this group to the extent of 9 per cent demonstrates the reality of the "extinction of the allergy," since such calcifications do not appear to have any relation with the coccidioidine histoplasmine allergy recently tested by us, while they do respond to BCG with shortening of the pre-allergic period, which seems to indicate that we should classify them among the latent allergies, or hidden allergies according to Willis-Sayé

2) The reactors with one or two plus reaction (5 to 9 mm and 10 to 19 mm) as well as the reactors to the second test, and the so-called doubtful reactors (less than 5 mm) reveal 2-3 per cent of lung or lymph node lesions, while those with 3 or 4 plus reaction (more than 19 mm or a phlyctena) show 8 10 per cent of the same type of lesions

B) *Radiographic Results* Among 5,000 radiographies which were taken as a result of suspicions arising from the microfilm, 29 per cent corresponded to lesions originating in tuberculosis, 34 44 per cent to residual forms and 32 53 per cent to cardioaortic lesions or other costal, lung or mediastinal abnormalities of different kinds. For every three microfilms one corresponded to tuberculous lesions, one to sequelae and the remainder to the anomalies mentioned.

Among the different clinico-radiological classifications of tuberculosis we have preferred to use that of the Spaniard Diez Fernandez because of its greater suitability to our needs. We have effected some slight modifications, without altering it in its essence, in order to try to simplify its application. For the sake of brevity we shall only present the lesions in their corresponding principal groups

I-A—lymph node forms, 35 14 per cent

I-C—disseminating forms, 9 92 per cent

III-A—infiltrative forms, 26 8 per cent

AB—phthisic forms, 28 11 per cent

If we consider that the first two groups cited correspond to children and young people, we find that 45 per cent correspond to infantile form classified as "primary infection," while 55 per cent correspond to adult phthisic forms or "reinfection."

Among the so-called primary infection the hilar lymph nodes were present to the extent of 54 32 per cent, the tracheobronchial lymph nodes 33 96 per cent and enlargements of the lymph nodes accompanied by infiltrative lesions, 10 86 per cent. Among the so-called haematogenous dissemination 5 per cent correspond to miliary forms, 60 per cent to partial dissemination in one or both lungs, and 35 per cent to pleural forms.

Among the infiltrative forms, which are considered as the be-

ginning of tuberculosis in adults, 28 per cent are cases with cavity formation at the time of the first examination and 72 per cent are still free of cavity formations. Among the phthisis forms the caseous exudatives and their lobar and lobular forms account for 5.63 per cent, proliferatives 57.92 per cent, the destructives 11 per cent and the fibrocaseous 25.23 per cent.

As can be seen any one of the anatomoclinical types of tuberculosis can appear without clinical symptoms and become a radiological discovery in the "apparently healthy."

Prophylaxis by means of the mass x-ray examination is thereby carried out in all the pulmonary forms of tuberculosis and, with the exception of the phthisic forms, in which the possibilities of cure are very remote, as well as the fatal disseminating forms, we can expect genuine success in 81 per cent of the cases of discovered lesions, in which are included the lymph node, infiltrative and partial disseminating forms.

### C) *Laboratory work in the diagnosis of latent lung tuberculosis*

The direct examination of the sputum and the blood sedimentation rate is referred to exclusively.

#### a) *Acid-fast bacilli and expectoration in relation to lung lesions*

III Am ( <i>Infiltrative Lesions</i> )	Cases	Percentage
With sputum with bacilli	5	16.6
(48 per cent) Without bacilli	25	
Without sputum	34	
III An ( <i>Infiltrative cavity forms</i> )		
With sputum with bacilli	27	45.0
(83 per cent) Without bacilli	32	
Without sputum	12	
III Bo ( <i>Caseous exudative phthisis</i> )		
With sputum with bacilli	4	66.6
(66 per cent) Without bacilli	2	
Without sputum	3	
III Bp ( <i>Proliferative phthisis</i> )		
With sputum with bacilli	10	22.0
(61 per cent) Without bacilli	35	
Without sputum	29	
III Bq ( <i>Destructive phthisis</i> )		
With sputum with bacilli	8	66.0
(93 per cent) Without bacilli	4	
Without sputum	1	
III Br1 ( <i>Common fibrocaseous phthisis</i> )		
With sputum with bacilli	31	69.0
(81 per cent) Without bacilli	14	
Without sputum	6	

Sputum is present in 83-93 per cent of the cavity formations and in a half or perhaps rather more than a half of the infiltrative and phthisic forms of the disease. The direct examination of sputum shows a positivity of 16.6 per cent in the simple infiltrative forms, 45 per cent in those forms with cavities, 22 per cent in the proliferative phthisis, 66.6 per cent in broncho-pneumonic phthisis, 66 per cent in the destructive forms and 69 per cent in the fibro-caseous lesions.

b) *Blood sedimentation rate in relation to lung lesions*

III Am ( <i>Infiltrative Lesions</i> )	Cases	Percentage
Up to 10 mm	24	36
11-30 mm	31	47
31-70 mm	10	15
More than 70 mm	1	1.5
TOTAL	166	

III An (*Infiltratives with cavity formations*)

Less than 10 mm	6	16
11-30 mm	10	26.6
31-70 mm	17	44.5
More than 70 mm	5	13.3
TOTAL	38	

III Bo (*Exudative caseous phthisis*)

Less than 10 mm	2	22.2
11-30 mm	3	33.3
31-70 mm	1	11
More than 70 mm	3	33.3
TOTAL	9	

III Bp (*Proliferative phthisis*)

Less than 10 mm	21	33
11-30 mm	13	36.5
31-70 mm	18	29
More than 70 mm	1	1.74
TOTAL	53	

III Bq (*Destructive phthisis*)

Less than 10 mm	1	11
11-30 mm	2	22.22
31-70 mm	3	33.33
More than 70 mm	3	33.33
TOTAL	9	

III BrI ( <i>Common fibrocaceous phthisis</i> )	Cases	Percentage
Less than 10 mm	11	28
11-30 mm	8	21
31-70 mm	9	23
More than 70 mm	10	26
TOTAL	38	

As can be seen the blood sedimentation rate appears as normal in 36 per cent of the infiltrative and proliferative forms, 28 per cent in the fibrocaceous lesions, 16 per cent in the infiltratives with cavity formations and 11 per cent in the destructive forms. Although without diagnostic value this goes to show the stage of toxic repercussion of the disease in the organism.

*D) The contribution of successive surveys to the Pathogenesis of tuberculosis*

Having taken out of our files at random 8,113 index cards of persons of both sexes whose ages ranged from 2-60 years who had been examined at intervals of one or two years, most of them twice, some three times and, very exceptionally, four times, we made a brief study of the tuberculin reactions and the appearance of lesions. This served to demonstrate the following:

Allergic fluctuation is a common occurrence. Allergy appears in 80 per cent of nonreactors within the term already mentioned. Allergy, also, attenuates, dies out or exacerbates itself. The loss of allergy is an undeniable fact and its frequency was found to be 0.28 per cent among hyperergics (+++ and ++++), 2.4 per cent among allergics with two plus reaction, 5.1 per cent among those with one plus reaction and 9 per cent among hypoergics. This gives the impression that the aforesaid loss comes about gradually.

Nonreactors show lesions without the reaction having varied to the extent of 1.33 per cent which are limited to a large amount of the lymph nodes (pre-allergic period), when a positive change occurs of this group show lesions (primary lesions?), distributed among enlarged lymph nodes (93 per cent) and pulmonary infiltrations (7 per cent).

Lesions which appear among allergics with or without change in their respective tuberculin tests show a frequency of 1.06, 1.29, 1.09 and 3.40 per cent among hypoergics and allergics with 1, 2 or 3 plus reaction respectively. Enlargement of the lymph nodes predominate overwhelmingly over the infiltrative, disseminating, pleuritic and phthisic forms as the first radiographic manifestation of the disease.

It does not seem to be the primary complex nor the pleural

reaction but the adenopathy which is the first detectable lesion before and during the development of the allergy. This leads us to think that the "complexes" are in reality advanced radiological stages of the lesion. Nor can discrimination be made in the adult between first infection and reinfection upon the basis of the anato-mo-radiological lesions even when prior results of tuberculin tests of the individual had been known.

### *Treatment*

The treatment of the latent lesions could not be appraised among us because of the only recent inauguration of a well-equipped Tuberculosis Sanatorium in our midst. Good preventive results were obtained among normergics with B C G vaccination.

### *Prognosis*

Prognosis of latent pulmonary tuberculosis is presented from the point of view of the spontaneous evolution of the lesions (without active collapse therapy or sanatorium treatment) and of its "quoad vitam" significance.

a) *The lymph node enlargements* recede in 84.2 per cent, remain stationary in 12.8 per cent and evolve, presenting infiltrative (1.4 per cent) and phthisic forms (1.4 per cent). *Minimal lesions* disappear to the extent of 40 per cent, remain stationary in 20 per cent and evolve in phthisic forms in 40 per cent. *Infiltrative forms* heal in 43 per cent, recede partially, leaving some nodules, in 15 per cent, and show pleural complications in 3.1 per cent, remain stationary in 43.7 per cent and evolve in phthisic forms in 7.7 per cent of the cases. Phthisic forms do not heal, but evolve in 92.9 per cent and recede partially in 7.1 per cent.

b) "*Quoad vitam*" prognosis. In order to study this we have consulted the tuberculosis mortality lists of the past six years in order to identify those deceased persons who figured in our register. Moreover, we have had recourse to our files in order to find the names of all those persons who died from tuberculosis during 1943-46.

In spite of possible errors accruing from the use of this technique we believe it to be of interest to publish the results obtained.

It can be said that the lymph node forms without concomitant lung lesion show a 100 per cent favorable life prognosis. Among the other forms, fibrocaseations show a high mortality figure (17 per cent) and are followed by caseous pneumonic phthisis (12.17 per cent), disseminating cases (4.24 per cent), infiltrations with cavity (5.25 per cent), infiltrative and productive cases (4.4 per cent), and the destructive cases (5.3 per cent). Deaths generally occur within two or three years or longer but rarely in the fourth

year whatever the form Eighty per cent of the deaths occur within the first two years

We desire to call attention to the fact that the prognosis for certain healthy allergies in 1, 2 or 3 years is no more favorable than that corresponding to the discovered lesions These cases account for about 60 per cent of the total of deaths from tuberculosis in our midst They form a part of what Flatzek preferred to style "additional mortality" and as far as our case is concerned we share his opinion, by which we mean to say that they are a result of precarious means of livelihood and poverty

### GENERAL CONCLUSIONS

1) Tuberculosis case-finding among apparently healthy individuals should be carried out systematically by means of (a) community examination, (b) examination of the family and known contacts of tuberculous persons and (c) examination of admission cases to the general hospitals

2) In large cities the Community Examination should be carried out at fixed places which the general public can reach easily, while mobile x-ray equipment can be utilized to attend country people and the Army

3) Photofluorography (35 mm) is the most economic and efficient method of discovery of latent, endothoracic lesions For this reason alone, its originator, Manuel de Abreu, should have his place among the benefactors of humanity

4) Tuberculin reaction will demonstrate the existence of tuberculous infection and its use should be the rule in the clinical and epidemiological study of tuberculosis

5) The standard x-ray picture will decide in every case whether tuberculous lesions which had been suspected from the roentgenphotograph really exist, but only the clinic and the complementary elements of the laboratory can decide definitely what is the diagnosis and its importance

6) The Community Examination should not stop at the discovery of new sources of the disease, but should contribute towards its control and treatment by making the cases known and sending them to specialists in phthisis or a tuberculosis center

7) Since the roentgenphotographic-tuberculin method is practically infallible in the examination of healthy normergics, the subsequent use of BCG vaccine is extremely valuable as a final prophylaxis measure

8) The Card Index File and the Register of Results should merit special attention They serve as sources of statistical information and of investigation and also cut out a great deal of routine work



TUBERCULIN TESTS — 105,858 Cases

Age	0-5		6-10		11-15		16-20		21-30		31-40		41-50		51-60		Over 61		Total	Total
Sex	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Male	Female
1941	40	56	72	124	262	311	685	612	1525	1097	1088	555	614	264	375	155	110	31	4771	3205
1942	32	32	79	144	914	712	2062	1901	4663	2693	3140	1089	1006	288	570	134	169	33	12635	7026
1943	56	56	288	387	1546	1196	2416	1787	3746	2262	2572	1097	1403	619	885	283	300	77	13212	7764
1944	66	70	100	160	1179	825	2137	1757	3795	2267	2371	1084	1216	509	762	233	281	87	11907	6992
1945	31	29	56	107	1057	764	2186	1776	3631	2032	2509	926	1440	501	883	201	307	71	12100	6407
1946	55	70	209	256	1105	910	2355	1601	4118	2042	2670	1012	1550	554	793	179	300	60	13155	6684

PERCENTAGE TOTAL OF REACTORS — According to age and sex

Age	0-5		6-10		11-15		16-20		21-30		31-40		41-50		51-60		Over 61		Total	Total
Sex	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Male	Female
1941	57.5	62.3	80.0	71.7	94.3	92.4	94.4	96.1	98.1	97.1	99.1	98.0	99.5	97.7	99.2	99.1	99.6	100.0	97.3	95.0
1942	78.0	81.2	78.4	80.4	93.8	90.0	95.5	95.0	97.3	95.1	97.4	97.1	96.1	96.5	98.5	99.1	95.1	100.0	96.5	94.2
1943	53.5	44.6	67.3	72.0	85.8	81.3	89.3	87.2	93.1	91.1	97.0	95.4	96.5	95.6	96.7	95.6	98.3	98.6	91.5	88.7
1944	86.3	78.5	84.0	85.0	94.2	93.2	96.2	93.3	97.1	96.3	98.6	97.5	98.9	97.1	98.6	98.1	98.3	97.9	97.6	95.6
1945	61.2	75.8	67.5	59.4	87.7	79.0	91.6	86.5	96.6	94.0	97.0	96.0	98.0	97.0	97.0	97.5	95.0	98.0	94.5	90.5
1946	61.8	47.0	73.0	72.9	85.3	81.6	93.6	88.3	97.4	92.5	97.8	96.2	98.6	97.0	98.5	95.4	99.0	98.2	95.4	89.9

PERCENTAGE REACTORS TO 0.1 MILLIGRAM S.O.T. (first mantoux)

Age	0-5		6-10		11-15		16-20		21-30		31-40		41-50		51-60		Over 61		Total	
Sex	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Male	Female Total
1941	250	320	580	459	795	748	805	778	921	849	953	875	965	937	952	921	960	937	903	816 809
1942	687	687	607	617	785	714	787	760	846	812	894	866	903	888	930	939	892	970	850	799 831
1943	357	250	420	433	616	563	657	638	768	711	841	797	851	780	870	832	880	856	750	679 727
1944	757	714	750	730	847	831	876	827	910	893	949	940	958	938	947	947	944	957	916	883 904
1945	483	689	515	474	767	640	806	755	900	850	930	900	930	900	930	925	920	950	875	810 850
1946	400	242	440	413	537	558	725	652	850	742	895	828	916	851	890	849	900	832	813	705 780

PERCENTAGE HYPERERGIC REACTORS (3 and 4 plus reactors)

Age	0-5		6-10		11-15		16-20		21-30		31-40		41-50		51-60		Over 61		Total	
Sex	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Male	Female Total
1941	50	17			45	38	30	43	47	37	43	35	47	37	72	38	80	64	46	36 42
1942	93	93	25	20	15	21	20	26	28	47	48	56	46	34	40	66	17	30	32	39 35
1943			40	69	39	48	30	48	49	61	71	87	63	70	56	45	40	26	50	59 53
1944	30	14	40	50	17	21	16	27	30	43	39	60	48	68	37	25	24	57	30	41 34
1945	32		35	84	12	11	16	24	21	34	34	52	43	42	30	25	13	14	25	32 21
1946			10	19	08	06	03	09	07	13	17	18	11	21	14	11	16	10	12	16

ABREU ROENTGENPHOTOGRAPHS—Total of Cases, 119,386

Age	0-2	3-5	6-10	11-15	16-20	21-30	31-40	41-50	51-60	Over 61	Total
Sex	M F	M F	M F	M F	M F	M F	M F	M F	M F	M F	Male Female Total
1941	24 39	38 47	182 330	302 707	708 809	1454 1131	1008 547	554 258	341 130	97 35	4708 4033 8741
1942	14 11	21 24	83 137	859 671	2003 1696	4200 2497	2919 1031	1604 528	997 216	367 58	13067 6869 19936
1943	15 18	52 45	351 450	1658 1232	2607 1975	4258 2619	2963 1236	1646 663	1047 324	369 98	14966 8660 23626
1944	29 25	61 70	125 194	1324 973	2557 1919	4267 2493	2677 1196	1347 598	883 264	344 101	13614 7833 21447
1945	7 8	32 38	92 133	1216 901	2385 2000	4091 2399	2881 1064	1643 548	1012 240	349 84	13708 7415 21123
1946	21 15	91 81	294 373	1422 1055	2873 1807	4956 2649	3208 1289	1894 674	1028 259	425 99	16212 8301 24513

PERCENTAGE LYMPH NODES AND CHILDHOOD TYPES OF TUBERCULOSIS

Age	0-2	3-5	6-10	11-15	16-20	21-30	31-40	41-50	51-60	Over 61	Total
Sex	M F	M F	M F	M F	M F	M F	M F	M F	M F	M F	Male Female Total
1941	125 128	105 85	38 42	10 14	15 13	08 04	02 09		03		091 134 111
1942	357 455	143 208	97 117	16 25	07 05	05 04	04 05	02	04 09		063 097 078
1943	200 62	96 159	46 37	18 13	10 03	04 03	02 02	006 01			072 071 072
1944	34	100 57	88 31	18 20	14 09	11 09	09 06	09 13	06 04		126 113 121
1945	143 125	52	76 52	100 08	03 04	04 02	01 06	02	01 04	02	040 052 044
1946	380 133	87 86	47 40	07 08	01 02	002 007					027 049 037

# PERCENTAGE OF MINIMAL LESIONS

Age	0-2	3-5	6-10	11-15	16-20	21-30	31-40	41-50	51-60	Over 61	Total		
Sex	M	F	M	F	M	F	M	F	M	F	Male	Female	Total
1941			05	03	05 05	03 01	05	07 04	07		042	019	032
1942				03	03 03	08 03	03 05	05 02	09 04	05	058	027	048
1943		19		03 03	05 03	04 02	04 03	02	05 06		039	025	034
1944	40			007 01	02 005	03 02	03 06	03 06	03	20 10	031	025	029
1945				008 01	01 01	01 02	02 01	01 05	04 04	03	017	018	017
1946			06 02	007 01	003 005	003 01	01			02	004	006	005

# PERCENTAGE OF GROSS LESIONS

Age	0-2		3-5		6-10		11-15		16-20		21-30		31-40		41-50		51-60		Over 61		Total		
Sex	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Male	Female	Total
1941			11	03	07		05	11	16	17	21	18	25	04	20	15	41	28	166	106	138		
1942	91		12		03	01	03	04	11	07	12	12	19	11	21	27	37	17	120	077	106		
1943			03		02	03	06	03	08	10	08	06	11	11	25	21	35	40	093	076	087		
1944					01	01	02	01	06	07	12	06	15	06	17	11	32	10	084	046	070		
1945					01	03	02	01	04	07	04	05	09	11	11		01	38	051	051	051		
1946	66		05		007	03	03	05	04	04	08	07	09	13	20	11	26	30	068	062	068		

in future examinations of the same patient as valuable time and films are economized

9) In order that the final object of the work being done and its appraisal can be further improved, connections should be maintained with other centers of prophylaxis, treatment and investigation of the disease

10) Although Sanitary Education should not be neglected, the Compulsory Health Card should be resorted to in order to ensure a rapid, uniform and comparative survey of the prophylaxis and epidemiology of tuberculosis in large cities

11) The Community Examination plays a manifest and rapid part in the decline of infection and tendency to tuberculosis. Its labor is backed up by BCG vaccination and modernization in the form of sufficient beds in the sanatoria destined for the purpose, and by the establishment of Social Insurance. In spite of this, however, additional tuberculosis mortality, which accounts for 60 per cent of the total tuberculosis mortality among us, can only be checked by means of economic and social measures which regulate and guarantee the most elementary needs of the people

### CONCLUSIONES GENERALES

1) El descubrimiento de casos de tuberculosis entre personas aparentemente sanas debe ser llevado a cabo sistemáticamente por medio de (a) examen de la colectividad, (b) examen de la familia y de los contactos conocidos de personas tuberculosas y (c) examen de los casos admitidos a los hospitales generales

2) En ciudades grandes el Examen de la Colectividad debe llevarse a cabo en lugares fijos, a los que el público en general puede acudir fácilmente, mientras que el equipo radiográfico móvil puede ser utilizado para servir a la gente del campo y al Ejército

3) La roentgenofotografía (35 mm) es el método más económico y eficaz de descubrir lesiones endotorácicas latentes. Basta esta razón para que su inventor, Manuel de Abreu, ocupe un lugar entre los benefactores de la humanidad

4) La reacción a la tuberculina demuestra la existencia de la infección tuberculosa y debe emplearse siempre en el estudio clínico y epidemiológico de la tuberculosis

5) La película radiográfica regular decidirá en cada caso si verdaderamente existen lesiones tuberculosas que se habían sospechado en la roentgenofotografía, pero sólo los hallazgos clínicos y los exámenes complementarios de laboratorio pueden decidir definitivamente cuál es el diagnóstico y qué importancia tiene

6) El Examen de la Colectividad no debe terminar con el descubrimiento de nuevas fuentes de la enfermedad, sino que debe contribuir a su control y tratamiento. Con este objeto se deben

dar a conocer los casos y se debe mandarlos a especialistas en tisis o a centros para tuberculosos

7) Ya que el metodo roentgenofotografico-tuberculinico es virtualmente infalible en el examen de los normergicos sanos, el empleo subsiguiente de la vacuna B C G es sumamente valioso como medida profilactica final

8) El Archivo de Tarjetas de Índice y el Registro de Resultados deben merecer atencion especial pues sirven como fuentes de informacion estadistica y de investigacion y eliminan, tambien, mucho trabajo rutinario en exámenes futuros del mismo paciente, economizando asi valioso tiempo y peliculas

9) Para alcanzar el objeto final de la labor que se lleva a cabo y para su mejor valuacion, deben mantenerse relaciones con otros centros de profilaxia, tratamiento e investigacion de la enfermedad

10) Aunque no se debe descuidar la Educacion Sanitaria, se debe recurrir a la Tarjeta de Salud Obligatoria a fin de asegurar un censo rápido, uniforme y comparado de la profilaxia y epidemiología de la tuberculosis en las grandes ciudades

11) El Examen de la Colectividad desempeña un papel claro y rapido en la disminucion de la infeccion y la tendencia a la tuberculosis Respaldan su labor la vacunacion con B C G, la modernización, en la forma de suficientes camas en los sanatorios destinados para este proposito, y el establecimiento del Seguro Social Sin embargo, a pesar de esto, la mortalidad por la tuberculosis, que entre nosotros es responsable por el 60 por ciento de la mortalidad total, solo puede ser combatida por medio de medidas económicas y sociales que regulen y garanticen las necesidades más elementales de nuestra gente

# Bagasse Disease of the Lungs\*

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The product remaining after extraction of sugar from sugar cane is called *bagasse*. This material is frequently burned, either as fuel or for disposition, but in some areas is baled for future conversion, by processing, into insulating and acoustic board. It may remain in the field for some months before use.

In 1941 Jamison and Hopkins<sup>1</sup> reported pulmonary disease presumably resulting from inhalation of bagasse dust. In 1942 Castleden and Hamilton-Paterson<sup>2</sup> and Gillison and Taylor<sup>3</sup> reported six additional cases. In 1943, Sodeman and Pullen<sup>4</sup> reported a case with needle biopsy of the lung and described a section of the lung of another patient who had died of the disease. In 1944 the same authors<sup>5</sup> summarized the findings in eleven cases, including the biopsied case reported in 1943. They discussed the possible etiologic factors underlying the pulmonary picture, and, in a separate report with Pinto and Pearson,<sup>6</sup> demonstrated the relative unimportance of the silica fraction. In the same year Jamison, Bryan and Day<sup>7</sup> reported an additional case, bringing the total number on record to twenty. The present report concerns the findings in four additional patients.

All cases previously reported have occurred in men. One of the present group is that of a colored female, thirty-four years of age, who gave a history of long continued exposure to dust arising from insulating board *after* processing. Her history does, however, include exposure to the dust of bagasse before processing. In none of the other cases cited has the pulmonary picture been noted following exposure to dust after processing, and, since this patient had been exposed to both types of dust, a claim of disease appearing after exposure to processed dust cannot be made.

The outstanding clinical findings are summarized in Table 1.

As in the group previously reported,<sup>5</sup> sex and age depend on selection of workers in bagasse. Only one case (Case No. 2) was a female, and the ages varied from twenty-six to fifty-seven. All were Negro. Length of exposure before the development of symptoms varied from four to seventy-eight weeks, but in three of the

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# SUMMARY OF CLINICAL DATA ON CASES REPORTED

Case No	Age	Race	Length of Exposure (Weeks)	Cough	Dyspnea	Sputum	Hemoptysis	Night Sweats	Chills and Fever	Loss of Weight (Pounds)	Pharyngeal Irritation	Duration of Symptoms before Admission (Weeks)	Cyanosis	Examination of Chest	Röntgenologic Picture of Chest	Days of Hospitalization	Follow-up
1	57	C	10	+	+	+	-	+	+	30	+	6	+	Rales over both bases posteriorly	A mottled infiltration of both lung fields spreading from the hilum to the periphery	3	Death with autopsy
2	34	C	78	+	+	+	-	+	-	15	+	8	-	Vocal fremitus increased with B-V breathing right lung posteriorly	As above	7	Complete clearing
3	26	C	4	+	+	+	-	-	-	Amt ?	+	3	-	Fine rales scattered throughout both lung fields	As above	2	Complete clearing
4	42	C	8	+	+	+	+	+	+	Amt ?	-	4	-	Fine rales throughout both lung fields	As above	9	Lungs almost clear to roentgen-ray in two months



four instances fell in the usual range of three weeks to two months

Symptomatically, cough, dyspnea, and production of sputum, were outstanding findings. Dyspnea appeared suddenly, as a rule, and became sufficiently severe to force the patient to bed. Hemoptysis occurred but once in this group and generally is uncommon. The sputum was scant and mucoid with a whitish appearance. Fever, at times with chills, was found in two patients. In general the fever curves and respiratory and cardiac rates followed the trend described in the previously reported series of eleven cases.<sup>5</sup>

Examination of the chest revealed findings which were not striking, and which were meagre in proportion to the roentgenologic picture. Scattered and patchy rales with minor changes in breath and voice sounds were heard. The roentgenologic findings were those of a bilateral mottling more dense in the hilar regions. Invariably clearing of the process was found in the follow-up examinations.

Previous studies have disclosed<sup>5</sup> that tubercle bacilli are not found in the sputum, even with concentration methods. Fungi have not been found consistently, and bronchoscopy has shown little. The sputum has shown, in general, a cellular content of both polymorphonuclear leukocytes and lymphocytes. Eosinophiles have been absent. In the blood, moderate leukocytosis is the common finding, with slight shifts to the left. Sedimentation rates are increased and, later on in the clinical picture, mild increases in the hematocrit and red blood count have been observed. Blood cultures, agglutination reactions for typhoid, paratyphoid, tularemia, and undulant fever have been negative. The present four cases conform to these findings. The Mantoux test has not been consistent. In the four cases now reported, two were negative, one positive, and in one case was not done.

Treatment has consisted primarily of bed rest during the acute stage of the disease together with supportive and palliative measures.

The clinical picture, as described above, represents the major findings as seen in our institution. It should be emphasized that only those patients have been seen who have sufficiently severe complaints to seek hospitalization. It is likely that a more mild clinical picture occurs, and, possibly, roentgenologic evidence of pulmonary involvement without symptoms at all. Surveys of workmen in bagasse would be necessary to establish these findings and the author has not had the opportunity to carry out such a survey.

The cause of the clinical picture is unknown. The relationship between work in raw bagasse dust and the development of the symptoms seems clear. The close association between the patient's

work and the characteristic clinical picture, with the absence of the picture under other circumstances, points to a definite cause and effect relationship between exposure to the dust and the development of symptoms

Various causes have been suggested Jamison and Hopkins<sup>1</sup> isolated a fungus from the first patient reported In one instance reported by Sodeman and Pullen<sup>5</sup> monilia were found in the sputum but were considered contaminants Attempts to isolate a fungus from the sputum have not met with uniform success<sup>2 3</sup> Bagasse itself is difficult to study After lying in the field for variable lengths of time, with fermentation and fungous and bacterial invasion taking place in the bales, bagasse is a complex substance not easy to analyze Fungous disease of the lungs of occupational origin is well known, as exemplified by the maple-bark disease<sup>8</sup> Exposure to dust after processing has not yet been shown to produce the picture, and such processing includes heat treatment which would destroy living agents Then, too, fungous infection, arising from bagasse, has been demonstrated by Morales-Otero and Koppisch<sup>9</sup> These observers in 1933 reported an epidemic in young chicks exposed to bagasse The disease was characterized by dyspnea, somnolence, drooping of the wings, loss of weight and fluffing up of the feathers, and death occurred in five days to two weeks Pulmonary changes were noted in which *Aspergillus fumigatus* was found both in lung sections and by isolation These authors were able to reproduce the disease In 1946 Gerstl, Tager and Marinaro<sup>10</sup> also reported the isolation of *Aspergillus fumigatus* as well as other organisms from raw bagasse and were able to reproduce in rabbits and guinea pigs, by both intravenous and intratracheal inoculations, a pulmonary disease in which *A. fumigatus* was recovered There is the possibility that these pictures represent the counterpart of bagasse disease in humans Comparisons of the lesions in these animals with those in human lung are now being made by Gerstl and his co-workers However, in bagasse disease in humans, no fungus has been consistently isolated and there is as yet little evidence to support a fungus as the causative agent Nevertheless, an infectious theory cannot be disproved on negative or indirect grounds

The picture is unlike that of byssinosis<sup>5</sup> as it occurs in workers with low-grade stained cotton An allergic theory has been proposed<sup>2</sup> and has been discussed at length elsewhere<sup>5</sup> Tuberculosis, suspected especially because of the roentgen appearance of the lungs, has been eliminated as the etiologic agent

Pneumoconiosis is a possible cause Bagasse contains five to seven per cent silica (silicon dioxide), but the clinical picture, including the resolution of the process, is unlike that of silicosis

Sodeman, Pullen, Pinto and Pearson,<sup>6</sup> in experimental studies with bagasse, have shown reactions in the peritoneum of the guinea pig indicating the relative unimportance of the silica fraction. Sodeman and Pullen<sup>5</sup> have demonstrated, in biopsies of the lung during the height of the clinical picture, as well as in a section of lung taken from patient No 1 of the present report,<sup>4</sup> spicules of a foreign material having the characteristics of bagasse and rotating polarized light as bagasse particles do. This evidence indicates that particles of bagasse do enter the alveolar regions and may initiate a reaction. However, the manner in which such particles may produce the changes remains obscure. Mechanical irritation alone, a reaction of the lung to a chemical product in the bagasse, as well as the introduction of a yet unrecognized infection, are all possibilities.

### SUMMARY

Report of four additional cases of bagasse disease of the lung re-emphasizes the characteristics of the clinical picture. Review of the evidence concerning the etiology of this picture indicates that the cause remains obscure.

### RESUMEN

Se informa sobre cuatro casos adicionales de la enfermedad pulmonar de bagazo, que recalcan de nuevo las características del cuadro clínico. El repaso de los datos pertinentes a la etiología de este cuadro indica que todavía queda oscura la causa.

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## D I S C U S S I O N

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One of the first things that impressed me in reading about this affliction was the importance of history taking, which is mighty important in tracing down a baffling diagnostic problem. If a patient comes to your office with cough and dyspnoea, you might ask him what work he does. If he says he has recently worked in a sugar cane factory you may have the solution of your problem. If you know what things to suspect, you have gone a long way on the road to a diagnosis.

I am not aware of ever having seen a case of bagasse disease, but, neither have I seen George Washington, but still I know a lot about him. I feel confident now, however, thanks to Dr Sode-man, that, if a bagasse victim came to my office I would make a correct diagnosis.

I was just thinking that it is about time to discover a disease that is curable. When we consider the present sick world with all its devastating afflictions, it's refreshing to be presented with a disease of which you can say with due dignity to the patient, "This, and not you, will pass away."

The continued search for new diseases is as vital to dynamic medicine as is the pursuit of new inventions in industry. By discovery of new diseases I mean, of course, mostly the unveiling of old afflictions in which the etiology, diagnosis and treatment have been on a speculation basis. History is full of instances where darkness clouded the true causative agent of disease. Pulmonary tuberculosis was once believed to be due to irritating secretions falling from the brain to the lungs. Appendicitis was considered as an intestinal colic. These are but brief examples of wise investigators, not satisfied with prevailing beliefs, tearing assunder theoretical speculations and putting truth in their places.

Let us not underestimate the importance of such contributions to medical knowledge that our main speaker has made. It marks another milestone along the road to better medicine and, therefore, improved humanity.

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# Syphilitic Heart Disease

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Syphilitic heart disease is a misnomer, for the basic lesion in syphilitic heart disease is an aortitis. This, in turn, consists of a perivascular lymphocytic infiltration of the vasa-vasorum in response to the invasion of the spirochete. Depending upon the extent and the degree of this infection within the aorta, we may have, complicating the basic lesion of aortitis, either aortic insufficiency, coronary ostial closure or aneurysm formation. It is most unusual to find a gummatous change within the myocardium or a diffuse lymphocytic infiltration of the myocardium. Rarer still is it to find in association with syphilitic heart disease myocardial infarction as a result of coronary ostial closure.

The diagnosis of aortitis per se is very difficult. It depends upon the history of syphilis or the finding of a positive Wassermann reaction. If the patient is under forty years of age, there should be a tambour aortic second sound and there should be no other complicating cardiovascular disease. The aorta should be widened upon roentgenographic or fluoroscopic examination. In addition, a widening of manubrial dullness and retromanubrial pain may also be present. Any combination of any three of these factors suggests the diagnosis of luetic aortitis. If we hold, however, to these criteria, we seldom make the diagnosis correctly. In fact, we more often diagnose the disease by simply stating that any patient with syphilis has aortitis. Because of the difficulty in the diagnosis of syphilitic aortitis, the material used in this study was selected from those cases of luetic heart disease that were proven at necropsy. In a series of essentially 10,000 necropsies performed by Dr. John F. Noble at the Ancker Hospital, there were 161 patients with proven syphilitic aortitis. Of this group 106 were white males, twenty-five of whom were under the age of fifty years, twenty-eight were white females, twelve under the age of fifty years (Fig. 1), twenty-one were colored males, ten under the age of fifty years, and eight were colored females, three under the age of fifty years. In the necropsy series at Ancker Hospital the ratio of white to colored necropsies is essentially 46 to 1 which suggests that syphilitic aortitis in the colored people has about the same incidence as that of the white people.

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Of this group of 161 individuals ninety-six had four plus blood Wassermann tests. Of the ninety-six, forty-nine had indeterminate spinal Wassermann tests in the sense that they were not completely positive, twenty-nine had four plus spinal Wassermann reactions, and the Wassermann test was negative in seventeen individuals. In forty-five of the 161 patients the blood Wassermann was indeterminate in that it was not completely positive. In this group the spinal fluid Wassermann in forty-three individuals was indeterminate and in two the Wassermann test was positive. There were nineteen of the 161 patients with negative blood Wassermann reactions eleven of whom had indeterminate spinal fluid Wassermann tests, two had four plus spinal fluid Wassermann tests and six had negative spinal fluid Wassermann tests. Contrary to the ordinary belief, syphilitic aortitis seems to be associated not infrequently with central nervous system syphilis, and the presence of central nervous system syphilis does not exclude cardiovascular syphilis.

In this group of patients with luetic aortitis, coronary ostial closure was rather common. It involved the right coronary artery in sixty-nine patients with complete closure of the ostia in eight patients, and in fifty of the sixty-nine patients the left coronary artery was also somewhat involved, but to lesser extent. The left coronary ostia was more involved in thirty-nine patients and there was complete closure in two. In this group the right coronary artery was also involved, but to a lesser extent. Valvulitis occurred

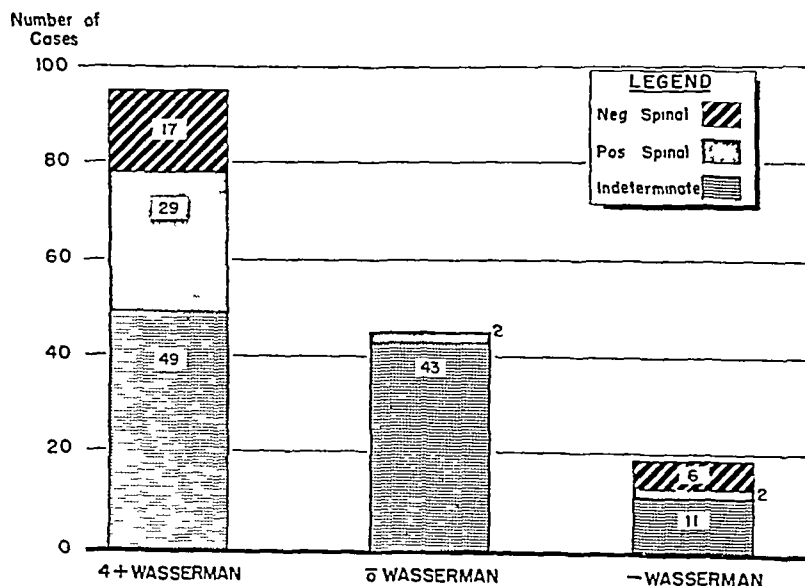


FIGURE 1 Wassermann Test Results

in eighty-five of the patients. Of eighty-five, thirty-two had valvulitis alone without aortic insufficiency, and in fifty-three individuals aortic insufficiency was present. There were eighteen patients who had miscellaneous complications in association with aortitis such as rheumatic heart disease, auricular fibrillation, hypertension and subacute bacterial endocarditis. In nineteen of the patients aortic aneurysm was present, and in fourteen of these the location of the aneurysm was described. Since the aneurysm involved more than one part of the aorta, the description of their location (Figs 2 and 3) would make it appear that there were more than fourteen aneurysms. The ascending aorta was involved eleven times, the transverse portion of the aorta five times, and the descending aorta five times. There were two aneurysms of the abdominal aorta, one involved the innominate artery and one the basal artery of the brain. Of the nineteen patients who had aortic aneurysms, fourteen had positive Wassermann tests, two had negative Wassermann tests, and in three the blood Wassermann was not recorded. In ten cases the aneurysm was an accidental discovery and there were no complications. In six cases the aneurysm ruptured, three times producing a cardiac tamponade, twice a bleeding into the pleural space, and in one case the rupture was retroperitoneal. In two of the patients there was a partial rupture of the aneurysm manifested by a superior mediastinal obstructive syndrome. In one patient there was an erosion into the esophagus which was characterized by the spitting of blood.

In thirty-seven cases the clinical findings and histories of rheu-

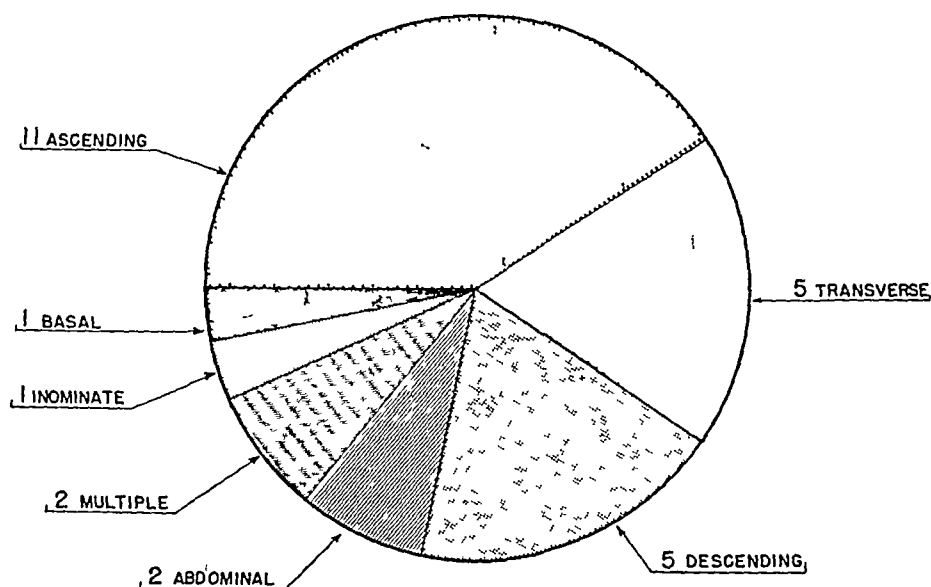


FIGURE 2 Location of aortic aneurysms (14 cases)

matic fever suggested the possibility of rheumatic heart disease. In these patients the correct diagnosis of luetic heart disease was made twenty-eight times and the correct diagnosis of an associated rheumatic heart disease was made twice. In five instances the patient was thought to have rheumatic heart disease when he had luetic heart disease, and in two instances he was thought to have syphilitic heart disease when the necropsy proved that he had luetic heart disease.

Of the entire series of patients it is interesting to note that syphilitic heart disease was the major cause of death in forty-one of the patients, and the causes of death from the anatomical standpoint were combinations of valvulitis, aneurysm and coronary ostial closure. In fifteen per cent of the patients or twenty-four individuals of the group, it was felt that the syphilitic aortitis with its complication played a contributing role in the cause of death. Here it was a combination of valvulitis and aneurysm formation. In ninety-six of the patients the syphilitic artery disease had no connection whatsoever with the cause of death. It was purely an accidental finding.

Rheumatic valve defects were present in fourteen patients. The aortic valve was involved five times, the mitral valve eight times, and the tricuspid valve was involved once. Bacterial endocarditis occurred in five individuals. It was implanted upon a previous

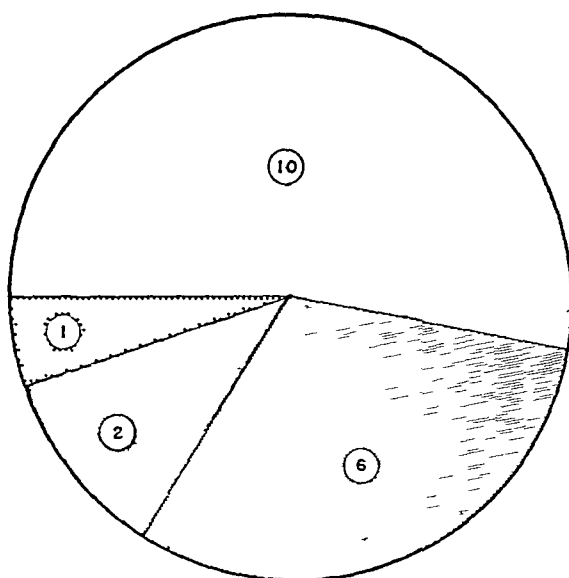


FIGURE 3 Complications in aneurysms (Total of 19 cases)

1 Erosion

6 Ruptured

2 Partial Rupture

10 Uncomplicated



rheumatic valve defect in four of the patients, and in only one instance was it upon a luetic defect. Auricular fibrillation occurred eight times, and in all of these patients some other complicating cardiac disease was present such as rheumatic heart disease or hypertension. Myocardial infarction as a result of closure of the coronary ostia occurred in three of the patients. In two of these individuals death was sudden. In one of the patients death did not occur until a clinical diagnosis had been made.

### SUMMARY

Of the 161 patients with syphilitic heart disease the following clinical facts were obtained:

- 1) In the diagnosis of syphilitic heart disease, one should obtain a positive Wassermann test or the history of syphilitic infection.

- 2) If we assume that the presence of a positive spinal fluid indicates an infection in the central nervous system, then, contrary to popular belief, central nervous system syphilis is rather common in syphilitic heart disease.

- 3) When the problem arises as to the etiology of the aortic valve defect, the following facts are important:

- (a) Whenever the physical findings are those of a stenosing lesion, then the lesion is rheumatic.

- (b) In the presence of a regurgitating type of lesion, the evidence seems to indicate that the lesion is probably luetic.

- (c) If we have a diastolic murmur at the apex in the presence of a frank aortic insufficiency and the heart is enlarged to the left, the diagnosis of mitral stenosis even in the presence of a history of rheumatic fever is hazardous. On the other hand, a diastolic murmur at the apex, in the presence of a frank syphilitic aortic insufficiency with the history of rheumatic fever and with the left ventricle not being enlarged, usually means an associated rheumatic mitral valve defect. The diagnosis is further supported if there is an associated auricular fibrillation.

- 4) Subacute bacterial endocarditis is rare in syphilitic heart disease, yet in five patients this phenomenon did occur. In four, the lesion was superimposed upon an associated rheumatic valve defect and in only one case upon a pure luetic valve defect.

- 5) The popular opinion that auricular fibrillation is unusual in syphilitic heart disease is widely held and yet, there were eight instances of patients suffering from syphilitic heart disease with auricular fibrillation. In every instance, however, the auricular fibrillation was associated with some complicating factor such as hypertension or rheumatic heart disease.

The results of the analysis of 161 cases of syphilitic heart disease

have been tabulated While the number is too small to be statistically significant, the analysis presents the pattern of the disease as it was seen at the Ancker Hospital

### RESUMEN

En un estudio de 161 pacientes con enfermedad sifilitica del corazón se obtuvieron los datos clinicos siguientes

1) Para diagnosticar la enfermedad sifilitica del corazon se debe obtener una prueba de Wassermann positiva o la historia de infección sifilitica

2) Si damos por sentado que la presencia de un liquido cefalorraquideo positivo indica una infección del sistema nervioso central, entonces, aunque contrario a la creencia popular, la sifilis del sistema nervioso central es bastante comun asociada con la enfermedad sifilitica del corazon

3) Cuando surge el problema de la etiologia del defecto de la valvula aortica, son importantes los siguientes hechos

(a) Cuando quera que los hallazgos fisicos indican una lesion estenosante, la lesion es reumatica

(b) Cuando existe una lesion de tipo de insuficiencia, la lesión es probablemente sifilitica

(c) Si se descubre un murmullo diastolico sobre el apice cuando existe una insuficiencia aórtica franca y esta hipertrofiado el corazón hacia la izquierda, es dudoso el diagnóstico de estenosis mitral aun si hay historia de fiebre reumática Por el contrario, un murmullo diastolico sobre el apice, cuando existe insuficiencia aórtica sifilitica franca y se obtiene la historia de fiebre reumatica y no esta hipertrofiado el ventriculo izquierda, generalmente indica un defecto asociado de la valvula mitral de origen reumático La presencia de fibrilacion auricular apoya aun mas el diagnóstico

4) La endocarditis bacteriana subaguda es rara en la enfermedad sifilitica del corazón, sin embargo, ocurrio este fenómeno en cinco pacientes En cuatro de ellos la lesión estaba superimpuesta sobre un defecto valvular reumático asociado y solo en un caso estuvo superimpuesta sobre un defecto valvular puramente sifilitico

5) La opinión popular de que la fibrilación auricular es rara en la enfermedad sifilitica del corazon es muy general, pero, a pesar de eso, hubo ocho casos de pacientes que padecian enfermedad sifilitica del corazón con fibrilación auricular Sin embargo, en todos los casos la fibrilación auricular estuvo asociada con algun factor complicante tal como hipertensión o enfermedad reumatica del corazón

# Pulmonary Mycoses\*

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The signs and symptoms caused by pulmonary mycoses are very much like those caused by pulmonary tuberculosis. The x-ray appearance of the lesions may simulate closely that found in tuberculosis. This explains in part frequent diagnostic errors. Hemoptysis and cough with thoracic discomfort are the most prominent symptoms. The diagnosis of mycosis can be established only by careful evaluation of the laboratory methods for the demonstration of fungi in the sputum, gastric contents, and drainages from sinuses and abscesses.

The collection of the sputum should be done as soon after awaking in the morning as possible. Before this is done, however, the teeth should be brushed, the throat gargled, and the mouth and throat rinsed. Every effort should be made to obtain only sputum from the lungs. Sterilized Petri dishes serve best for collection purposes. The fungi will most often be found in particles or flecks which are usually yellowish or gray in color. Freshly obtained specimens should be sent to the laboratory as soon as possible, where it is examined from direct smears or cultured or injected into animals. Methods and procedures are described in detail by Kurung<sup>1</sup>

## *Pulmonary Actinomycosis*

The term actinomycosis is applied to two groups of diseases of man and animals. In one group anaerobic *Actinomyces bovis* with the characteristic "sulphur granules" are observed in pus or tissues. They may be found in the gums and tonsils<sup>2,3</sup> of apparently healthy normal individuals. The second group includes aerobic *Actinomyces*, now called *Nocardia*,<sup>4</sup> a filamentous branching organism without any radial arrangement and without granule formation. Two recognized species of this group are *Actinomyces graminis* which is non-acid-fast and *Actinomyces asteroides* which is acid-fast. Proved cases of infection with *Actinomyces graminis* are rare. Pathogenic *Nocardia* have been isolated from the soil<sup>5</sup>. In general the sputum is thick, tenacious and grayish yellow in color with almost no odor. Frequently it contains no fungi, and they have to be obtained from "cold abscesses" and sinuses or microscopic examinations of tissue. The drainage from fistula has

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\*Read before the Fulton County Medical Society, December 4, 1947

no odor Local or generalized adenitis may be present Laboratory examination of the blood usually shows a low hemoglobin and red cell count The differential count shows an average of 70 to 80 per cent leucocytes, 2 to 10 per cent eosinophiles and 10 to 18 per cent lymphocytes

Roentgenograms may show any grade of infiltration of the parenchyma and involvement of the hilar glands Radiographic changes take place slowly and are usually followed by pleural involvement

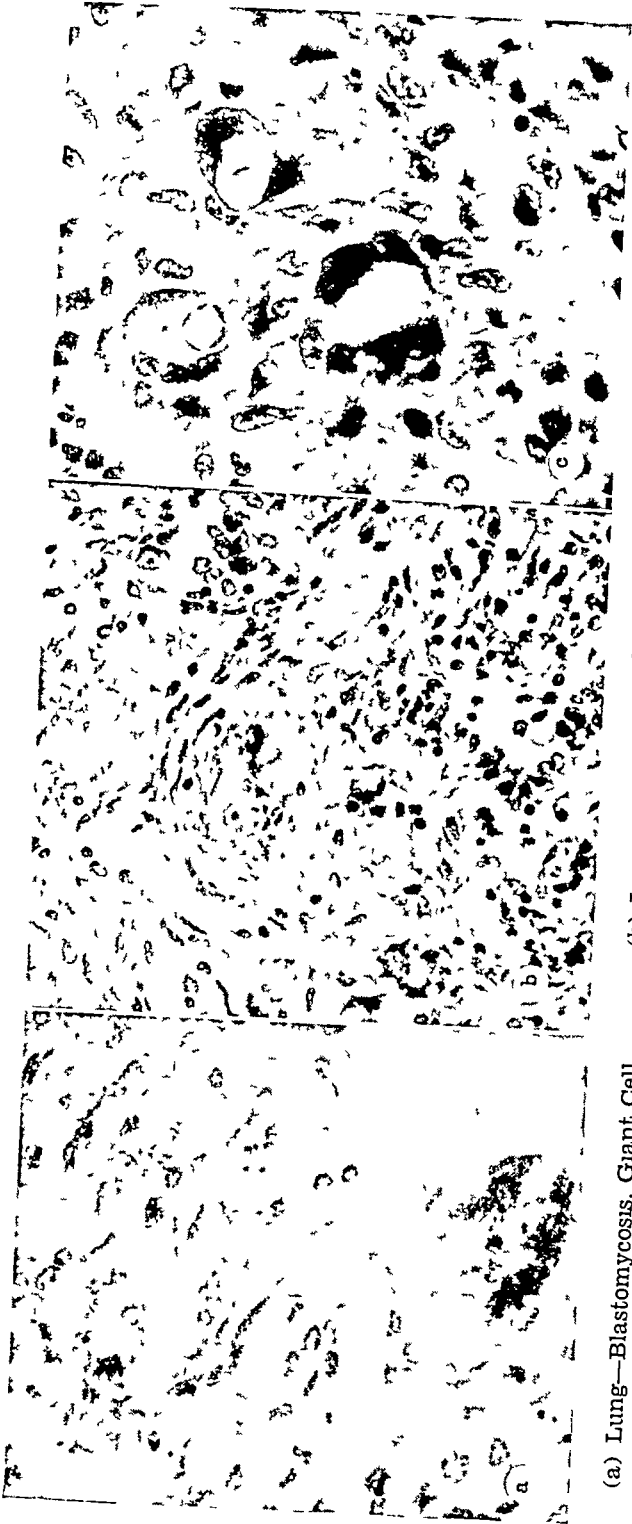
Treatment with penicillin has proven helpful in most cases, but many are recognized too late for this antibiotic to be effective Iodine and x-ray therapy are of doubtful value Strict bed rest, general supportive treatment, and cleanliness are also necessary aids

An interesting entity known as farmer's lung has been reported <sup>6</sup> It is clinically and radiologically a fairly well characterized disease The usual history is that a farmer, after working continuously for a time with mouldy hay from which a steamlike cloud of fungus-laden dust arises, develops a short dry cough with little or no expectoration, he may also suffer from general malaise, weakness and slight fever, but the outstanding feature is distressing dyspnea provoked by physical exertion Removal from exposure to mouldy hay dust is followed by rapid recovery, which is usually complete and permanent if further exposure is avoided With successive seasonal recurrences the disease tends to progress to chronicity, the cough becomes more productive, the abundant sputum is tenacious and frothy or purulent and slight hemoptysis may occur, physical weakness is marked and the dyspnea severe At this stage, the lung may show fibrosis, emphysema, and possibly bronchiectasis, and the x-ray picture is usually characteristic The relation of farmer's lung to inhalation of mouldy hay dust is unquestioned The commonly held view that it is a true pulmonary mycosis is based on the occupational history of the patient and the cultivation of moulds from his sputum The anaerobic species *Actinomyces bovis* was cultivated from the sputum in 2 cases In one of these the lesion appeared to be confined to the lung, but in the other case the lung infection, complicated by empyema, was part of a generalized disease which proved to be fatal

#### *Pulmonary Coccidioidomycosis*

A full historical report on this disease was made by Bass, et al <sup>7</sup> It is caused by *Coccidioides immitis* A detailed epidemiological investigation was carried out in four army air fields in the San Joaquin Valley, California by Smith and Beard <sup>8</sup> The investigation was based on coccidioidin testing permanent personnel and

FIGURE 1



- (a) Lung—Blastomycosis, Giant Cell
- (b) Lung—Blastomycosis x950
- (c) Lung—Blastomycosis x100

at first annually, later semi-annually, retesting the negative reactors. The pattern of geographic distribution of coccidioid endemicy showed an increase in the southern part of San Joaquin Valley with a decrease as one proceeds northward. Maximal incidence occurred in the arid dusty summer and autumn months. The seasonal infection rate showed that dust was the mechanism by which the fungus was transported. Grassing, paving roads and runways, and ultimately the use of highly refined oil on athletic areas were important local dust control measures. This control reduced infection rates from one-half to two-thirds.

Texas, Arizona, New Mexico, California and Argentina contain endemic areas. Arizona Indian children, living on reservations, have shown as high as 90 per cent positive reactions to the coccidioidin skin test. The author of this paper was also stationed in the San Joaquin Valley and saw large numbers of these cases in the terminal stage. The fatal cases are as tragic as death from malignancy.

The initial infection (incubation period, 5 to 20 days) is usually asymptomatic, but when symptomatic, the onset is sudden and comparable with influenza as, chills, fever, pleural pain, hemoptysis, sore throat, malaise, joint pain, headache, and cough (productive or nonproductive). The erythema nodosum and multiforme types of rash may be seen from the fifth to fifteenth day of the disease.

The secondary or disseminated form is frequently accompanied by subfebrile temperatures and great loss of weight. This form is found more often in the Oriental and dark-skin races, and in these races the mortality rate is much higher. Dissemination through the blood and lymph channels causes any of the organs of the body to be involved.

Positive diagnosis in both forms is made by finding the fungus by smear or animal inoculation. Other aids are a history of exposure in one of the endemic areas, and a positive skin test to a coccidioidin intradermal injection. This skin test should be considered in the same way and of the same value as the tuberculin skin test. Positive serological tests for precipitins and complement fixation are also helpful. A constant rise in titer suggests dissemination of the infection. Sensitivity is determined by the intracutaneous injection 0.1 cc of a 1:100 dilution of standard coccidioidin. A negative coccidioidin test to a 1:10 dilution is not unusual in the terminal stage of the infection.

Jamison<sup>9</sup> reports the predominant roentgen manifestations in coccidioid pulmonary infections which persisted for months or years following the acute initial phase of the disease as follows: (1) nodular parenchymal foci, (2) cyst-like cavities, (3) persistent

pneumonitis, (4) mediastinal and hilar adenopathy, (5) pleural effusion, (6) milary lung involvement, metastatic bone foci and other evidences of dissemination Negroes are about 100 times more likely to develop fatal disseminated coccidioidomycosis than white people White persons are more apt to develop a meningeal type of coccidioidal dissemination, while Negroes show a higher incidence of subcutaneous abscesses Dissemination, when it occurs late, appears to be of less ominous prognostic significance than when occurring within the first few days or weeks of the initial acute illness<sup>10</sup>

No specific treatment is of value Persistent cavity formation and hemorrhage are handled in the same manner as in tuberculosis Iodides, thymol, penicillin, copper and immuno-transfusions have all failed General supportive treatment should be used in every case Desensitization is difficult but should be tried and followed by iodide or colloidal copper

### *Pulmonary Blastomycosis*

Pulmonary Blastomycosis ("Gilchrist's disease") is usually a manifestation of a generalized fungus infection caused by *Blastomyces dermatitidis* which is more commonly found in the skin They occur in the lesions, pus, and sputum and appear as gram staining oval or round, thick walled bodies (7 to 10 micra) with fine granular protoplasm (Fig 1)

Usually the onset is insidious beginning with a mild respiratory infection A dry hacking cough, chest pains, slight fever and some dyspnea are usually present As the disease progresses all symptoms become more severe Loss of weight and strength become apparent Signs of toxemia or night sweats appear Later all organs of the body may be involved X-ray films usually show dense masses with irregular outlines Often the involvement of a rib at the same location suggests carcinoma Rarely early parenchymal lesions may be minimal with marked enlargement of the mediastinal nodes

The disease is often chronic in nature lasting for years in its cutaneous form, but in the pulmonary or systemic form, death usually occurs in 6 months to 3 years<sup>11 12</sup> A fatal outcome is expected in those having a high antibody titer (indicating extensive disease) and a negative or slightly positive skin test The prognosis is best in hypersensitive patients without complement fixing antibodies

Patients with definitely positive skin tests should be desensitized with vaccine or antigens before iodides are administered since a failure to desensitize may result in a lack of improvement or even a prompt exacerbation of the infection<sup>13</sup> Patients with

slightly positive skin tests may be successfully treated with large doses of iodides. Stock or autogenous vaccines should be administered until the patient has complement-fixing antibodies in the serum before administering iodides.

### *Pulmonary Sporotrichosis*

Sporotrichosis is a chronic fungus infection of the skin but does occur in the lungs. It is caused by *Sporotrichum Schenckii*, which is primarily a saprophyte or parasite of plants.<sup>14</sup> It is most commonly found in farmers, laborers and horticulturists. The pulmonary form is a manifestation of the disseminated type. Prognosis in this type is poor. Iodides are beneficial but must be continued long after all clinical symptoms have disappeared. X-ray therapy, surgery and vaccines are also used.

### *Pulmonary Coniosporiosis*

Smith<sup>13</sup> states that a peculiar type of pneumonitis, presumably allergic, occurs in laborers in the Northern forests who are repeatedly exposed to inhalation of spores of *Coniosporium Corticale* growing on the inner bark of maple logs. Recovery results when patient is removed from contact with the spores.

### *Pulmonary Moniliasis*

Probably the most common fungi are those which belong to the *Monilia* group. Treatment is difficult to evaluate because (1) the fungi appear to "go and come." Long periods elapse when they cannot be found, only to reappear both before and after treatment is started. (2) *Monilia* is usually considered to be an insignificant saprophyte in the respiratory tract. The author has seen numerous cases that have been pathogenic and caused acute illness. They may be the cause of bronchitis,<sup>15</sup> pneumonitis,<sup>16 18</sup> meningitis,<sup>19</sup> endocarditis,<sup>20 21</sup> and osteomyelitis.<sup>22</sup> (3) Many cases with fungus disease are hypersensitive to iodine which is the drug of choice. (4) The failure to determine the degree of sensitivity of the patient, and therefore, the failure to desensitize prior to iodides is another cause of ineffective treatment.

Bronchial infection sometimes disappears spontaneously, but often lasts for years with periodic progressions and retrogressions. X-ray films show nothing or slight peribronchial thickening and occasionally linear fibrosis. Parenchymal involvement is more rare and more serious than a bronchial infection. Elevated pulse and temperature, pleural pains, and an occasional effusion is present. The cough is severe and productive of mucoid, gelatinous sputum. A purulent sputum indicates a secondary infection. Pneumonic consolidation with the usual signs and symptoms may develop.



Death may occur when two or more lobes are involved with a pneumonic process

Hiatt and Martin<sup>23</sup> report a patient from whom *Candida albicans* was isolated from the sputum on numerous occasions. The patient was sensitive to iodides, and gentian Violet therapy caused an unfavorable reaction. The patient was treated with increasing doses of the immune rabbit serum and made a dramatic recovery.

Thrasher's lung<sup>24</sup> is caused by monilia and is characterized by a sudden onset with chill, fever, malaise, cough, and mucopurulent or bloody expectoration. Dyspnea is the most important and persistent symptom. Fine bronchial rales are heard over the bases, a slight leucocytosis is usually present, and the sedimentation rate is increased. Roentgenograms reveal pictures similar to miliary tuberculosis, but the fine mottling is densest in the parahilar regions and the bases, while the apices are relatively free. The x-ray signs may disappear or may result in patchy fibrosis with bronchiectasis. Similarities with sarcoidosis are especially to be noted, particularly in the presence of negative tuberculin reactions. Potassium iodide seemed to be of benefit, particularly in the milder cases, especially if the patients have not developed a hypersensitivity. Hypersensitive patients should be desensitized and treated cautiously. Intravenous gentian violet<sup>25</sup> has been used successfully in some acute pulmonary cases.

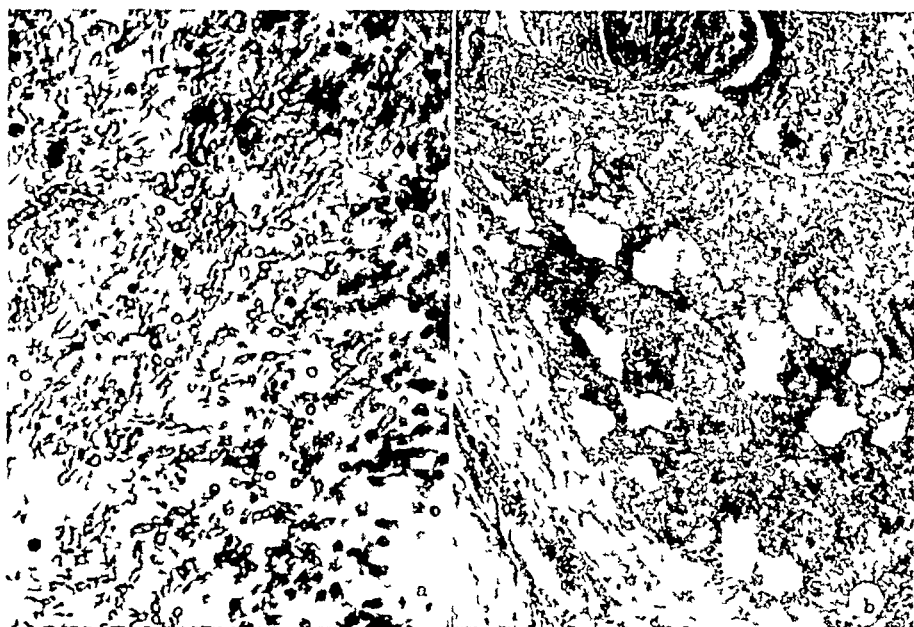


FIGURE 2

(a) Lung—Aspergillosis x700

(b) Lung—Abscess Aspergillosis x30

*Pulmonary Aspergillosis*

Squab feeders, fur cleaners and agricultural workers are especially prone to have the infection. Primary pulmonary aspergillosis is difficult to diagnose. Symptoms, signs, and clinical courses resemble pulmonary tuberculosis. However, aspergilli frequently are isolated from the sputum of patients with chronic bronchitis, intrinsic asthma and appear to be an accidental contaminant which gives no symptoms (Fig 2).

X-ray films may show smooth, dense lesions and cavity formation or they may show nodular diffuse shadows.

Iodides have been used with success. Hypersensitive patients should be desensitized. For the sake of completeness, penicilliosis and mucormycosis should be mentioned as similar to aspergillosis. Also, reference should be made to a case of pulmonary trichophytinosis reported by Denis, Hendtlass and Martin<sup>26</sup>.



FIGURE 3 Torulosis—X-ray of Lungs

Another rare fungus is *Geotrichum* which is described by Kuntstadter, et al,<sup>27</sup> who state that the genus is mostly saprophytic, but infections have been reported in man. This fungus causes symptoms of chronic pulmonary infection. Roentgenograms show peribronchial thickening and fine mottling in the mid-lung fields or in the bases. More severe cases present dense patches of infiltration with or without cavity formation. Iodides and vaccines are usually effective.

### *Pulmonary Torulosis*

Pulmonary Torulosis or Cryptococcosis is one of the fungus infections which has a tendency to invade the central nervous system. These patients may develop a generalized infection. Mildness may mask the infection for many months, and the only symptom may be a slight cough.

X-ray films in primary pulmonary infections show dense shadows resembling far advanced pulmonary tuberculosis or neoplasm (Fig 3). Cavities are not usually found nor is the mediastinum usually involved. Later milary lesions may be present. The author has used iodides and noted that the acute initial stage subsides into a quiescent stage which may flare up six months or a year later in an entirely different part of the body, finally terminating in central nervous system invasion. Reeves, Butt and Hammock,<sup>28</sup> and Smith<sup>13</sup> report a cure with sulfadiazine.

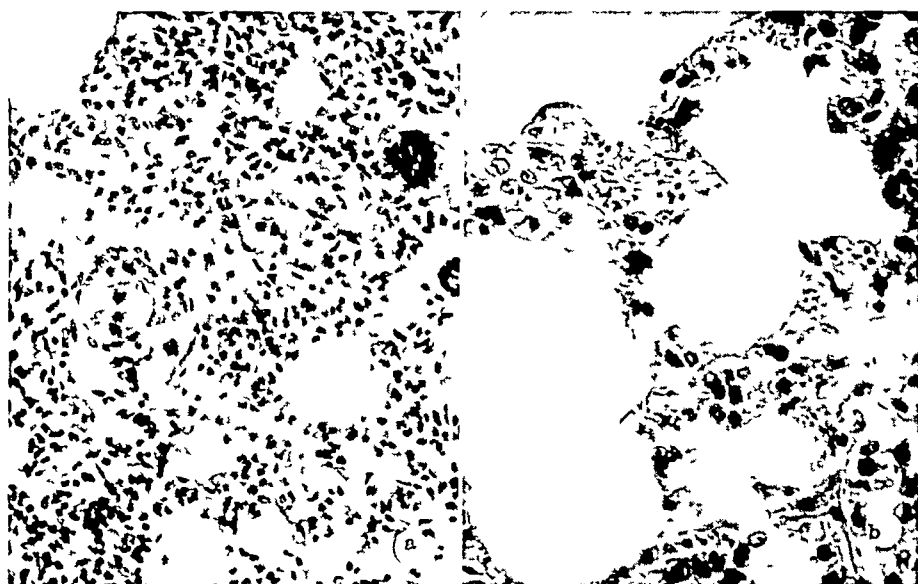


FIGURE 4

- (a) Lung—Histoplasmosis  $\times 330$
- (b) Lung—Histoplasmosis  $\times 810$

*Pulmonary Histoplasmosis*

The status of *Histoplasma capsulatum*, as related to pulmonary calcification in the human is still questionable. It is found in the cytoplasm of endothelial and mononuclear cells.<sup>28</sup> The Tuberculosis Control Division of the U S Public Health, in its annual report of 1946, mentions that such infections are probably responsible for pulmonary calcification observed in tuberculin negative reactors.

Young children are very susceptible to the disease which is characterized by fever, emaciation, anemia, leukopenia, splenomegaly and hepatomegaly. The literature<sup>30</sup> shows that one-third of the reported cases began in the ear, nose, lips, mouth, pharynx and larynx. Pulmonary manifestation was thought to be found usually in the disseminated or generalized cases but Smith,<sup>31</sup> Christie, Peterson,<sup>32</sup> and Palmer<sup>33,34</sup> have accumulated evidence that there may be a benign or primary pulmonary form that has been unrecognized which ultimately may result in pulmonary calcifications (Fig 4). In the disseminated stage, histoplasmosis is fatal. Treatment is unsatisfactory.

## CONCLUSIONS

The author has noted the frequent association of allergies with mycoses. Iodides are often not tolerated well by these patients. Chronic types of dermatitis are frequently aggravated.

Failure to desensitize hypersensitive patients, and the failure to establish complement-fixing antibodies in the patient are responsible for many of the failures in treatment of these diseases.

It is important to stress the similarity in signs, symptoms and roentgen findings between pulmonary mycoses and pulmonary tuberculosis. The care in making the correct diagnosis cannot be emphasized too greatly. Laboratory procedures must be easily available and adequate. Much time is required for continued culture of the fungi for correct identification.

## CONCLUSIONES

El autor ha notado la frecuente asociación de alergias con micosis. A menudo estos pacientes no soportan bien los yoduros. Frecuentemente se agravan los tipos crónicos de dermatitis.

La omisión de desensibilizar a los pacientes hipersensibles y la falta de descubrir anticuerpos de fijación de complemento en el paciente, son responsables por muchos de los fracasos en el tratamiento de estas enfermedades.

Es importante recalcar la semejanza entre los signos, síntomas y hallazgos roentgenológicos de las micosis pulmonares y la tuberculosis pulmonar. Debe hacerse gran hincapié sobre la necesidad

de hacer un diagnostico correcto Se debe contar con adecuados y disponibles procedimientos de laboratorio Se requiere mucho tiempo para el cultivo continuo de los hongos a fin de hacer la identificación correcta

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# Mediastinal Defect with Interpleural Communication Observed During Pneumothorax Therapy Report of a Case\*

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The phenomenon of interpleural communication is exceptionally rare,<sup>7 8 9</sup> only ten cases having been reported in the entire medical literature. It should be mentioned, however, that of these, two cases with mediastinal defects were found in patients without any tuberculous infection. One case reported by LeWald<sup>3</sup> in 1926 was of nontuberculous origin, no definite mediastinal defect having been proved, and as that author stated, "Evidently air had passed from the right pleural cavity into the left pleural cavity in some way, apparently through the upper portion of the mediastinum." The second unusual case, described in 1939 by Ochsner and De-Bakey,<sup>6</sup> presented a congenital mediastinal anomaly in a child of 18 months of age. They made their diagnosis of a left sided diaphragmatic hernia on the basis of fluoroscopic and x-ray studies, hernioplasty was contemplated. During the operation, however, they found, in addition to a defect in the left diaphragm, a complete absence of the anterior mediastinum. The pleural cavities presented one sac and both lungs could be inspected from a left sided surgical approach by removal of the seventh rib. We must say, therefore, that only eight cases of interpleural defects resulting apparently from tuberculous infection actually remain.

We have recently observed an unusual case with a defect in the anterior superior mediastinum associated with pulmonary tuberculosis in a young white male patient.

Before presenting our case, however, we feel that it is important to call attention to the fundamental anatomy of the mediastinum without going into detail. The weakness of the anterior superior chamber of the mediastinum is explained on the histological basis of the structure there being composed mostly of adipose and loose connective tissues which have replaced the atrophied thymus gland in the adults. Nitsch<sup>5</sup> as far back as 1910 in his studies of the mediastinal structure pointed out two anatomically weak places. One "weak spot" he found posterior to the upper portion of the sternum and the second "weak point" he found in the posterior inferior portion of the mediastinum near the level of the 8th rib.

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The case presented in this paper is almost similar to the cases reported by McCallum,<sup>4</sup> Julien<sup>2</sup> and Dumarest.<sup>1</sup> In our case there was also found a definite interpleural communication during pneumothorax therapy, the patient having very interesting sensations during the passage of the air through his mediastinal defect

### CASE REPORT

A.N.R., No 49,275, a white male, aged 31, was admitted to the Veterans Hospital Alexandria, Louisiana on June 19, 1947, by transfer from another hospital for further treatment of pulmonary tuberculosis

At the previous hospital the patient was treated for sinusitis and tonsillitis, and during the routine x-ray examination of the chest a minimal tuberculous lesion in the right upper lobe was found. Subsequent roentgenogram (Fig 1) taken a month later, on February 18, 1947, showed an extension of the tuberculous involvement in the right upper lobe and the sputum examinations were positive for acid fast organisms. Because of the progressive nature of the tuberculous lesion on the right side positive sputa, and age of the patient, artificial pneumothorax was induced on March 18, 1947, and this was maintained until time of admission to this hospital. During the third refill of air administered to the right side, patient stated that he experienced a sudden pain on the left side equivalent to a sensation of receiving pneumothorax bilaterally. An immediate x-ray examination of the chest disclosed bilateral marginal collapse.

On admission to this hospital patient was well developed and nourished and did not appear ill. Temperature, pulse and respirations were within normal limits and the blood pressure was 120/82. Physical examination of the chest revealed signs of bilateral pneumothorax, no rales or wheezes were audible. Roentgenological examination of the chest confirmed the physical findings. There was 15 per cent collapse of both lungs with thin apical adhesions on the right side, scattered nodular densities throughout the upper third of the right lung field, no evidence of cavitation. Routine sputum examinations as well as concentrates and cultures, have been consistently reported negative for tubercle bacilli. Urine and Wassermann examinations were negative. Sedimentation rate was 10 mm in one hour. Complete blood count revealed RBC, 4,820,000, WBC, 17,500. Hg, 13.9 grams, Polymorphonuclears, 87 per cent, Lymphocytes, 13 per cent. Repeated white blood count remained high up to 14,100. Blood chemistry showed normal findings.

It was felt that we were dealing here with one of two conditions either a congenital anomaly of the mediastinum or an unusual complication of a tuberculous infection. In either case the pneumothorax given on the right side would have passed through a weak spot or an opening in the mediastinum into the contralateral side. To substantiate the above observation careful fluoroscopic and roentgenographic studies of the chest were made on this patient prior to the pneumothorax refills and subsequent to it. The first x-ray film of the chest taken July 18, 1947 (Fig 2), showed about 10 per cent collapse on both sides, and the one following the refill of 300 cc of air (Fig 3) disclosed an increase





FIGURE 1



FIGURE 2



FIGURE 3

*Fig 1* Chest film, taken February 18, 1947, reveals tuberculous involvement on the right side. The infiltration seems to be exudative in character.—*Fig 2* Chest film, taken July 18, 1947, prior to pneumothorax refill, shows only 10 per cent collapse of both lungs. *Fig 3* Chest film, taken July 18, 1947, following the pneumothorax refill on the right side, shows an increase in the amount of the collapse bilaterally up to 30 per cent

to 30 per cent bilaterally To ascertain a to and fro passage of air through the mediastinum a refill was at this time given on the left rather than on the right side, yet here again an increase in the amount of collapse was noted bilaterally

On careful questioning of the patient for any special sensations in his chest during the time when the air passes from the right pleural cavity into the left side, he volunteered the following information "About 10 minutes after each refill I feel heaviness and pressure in the upper part of my chest which lasts for about 30 to 50 minutes" During this period, however, the patient did not show signs of difficulty in swallowing or breathing The fluoroscopic studies of the chest at that time showed a bilateral mediastinal bulge, which disappeared after the pneumothorax equalized in both pleural cavities

The atmospheric changes have been studied in both pleural cavities, prior, during and following a pneumothorax refill, by inserting simultaneously a needle connected with the pneumothorax machines to each side of the chest The following manometric changes have been registered The pleural pressures prior to refill on the right side was  $-5$ ,  $-1$ , and  $-3$ ,  $-2$  on the left side After 300 cc of air was injected into the right side, the manometric readings changed to  $-7$ ,  $+2$  on the right side and  $-4$ , 0 pressure on the left side

Keeping the needles in position for 10 minutes—during which time the patient was having the pressure sensations in his upper chest—the intrapleural pressures on the right side remained about the same, but on the left side the intrapleural pressure fluctuated more to the negative side to a final reading of  $-8$ , 0 It was also observed that patient required frequent refills to maintain a satisfactory collapse

It is interesting to note the vital capacity changes in this case following pneumothorax refill The capacity prior to pneumothorax was 2900 cc while a refill of 200 cc of air decreased the capacity to 2550 cc, in other words an unusual decrease of the vital capacity of almost twice the amount of air given

#### *Comment*

The symptoms, physical and roentgenological examinations in this case point unmistakably to a defect in the anterior superior mediastinum The defect appears to be of other origin than a rupture in the mediastinal walls from increased intrapleural pressures since the manometric readings were neutral or mostly negative This is a very interesting case of an interpleural communication resulting in a bilateral pneumothorax In about 40,000 pneumothorax refills given by the author during the last 10 years

he has never encountered a similar case

The question naturally arose as to further management of the case. After due consideration it was decided to abandon pneumothorax and keep the patient under close observation as far as his tuberculous lesion was concerned. The reasons favoring discontinuance of pneumothorax were as follows: (a) the lesion in the right upper lobe was of recent nature and exudative in character, (b) all recent sputum examinations were constantly negative for tubercle bacilli, (c) there is the danger of mediastinal emphysema in case of blockage in the passage of the air through the mediastinal opening, and (d) there is the possibility of pleural, and subsequent mediastinal effusion, or empyema, following infection during the course of pneumothorax therapy. Furthermore, in case of progression of the tuberculous infection in the right side a thoracoplasty will be performed just as Smith and Willis<sup>8</sup> did in 1929 in their case.

It is worthwhile to report that the patient at present is in excellent clinical and physical condition and that both lungs are reexpanding without complication.

### SUMMARY

- 1) An unusual case of mediastinal defect without apparent other organic anomalies is presented.
- 2) Only ten previous cases with similar defects are described in the medical literature.
- 3) Artificial pneumothorax induced on the right side caused transient bilateral herniation of the mediastinum with collapse of both lungs.
- 4) There was a definite to and fro passage of air during pneumothorax therapy given on either side.
- 5) The reasons for discontinuation of pneumothorax are here outlined.

### RESUMEN

- 1) Se presenta un raro caso de defecto mediastínico sin ninguna otra anomalía orgánica aparente.
- 2) En la literatura médica se han descrito solamente diez previos casos con defectos semejantes.
- 3) El neumotórax artificial que se aplicó en el lado derecho causó una hernia bilateral transitoria del mediastino con colapso de ambos pulmones.
- 4) Cuando se dio una insuflación de cualquier lado, el aire pasó de un lado al otro.
- 5) Se bosquejan aquí las razones por las cuales se discontinuó el neumotórax.

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# Cystic Disease of the Lung\*

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In the past ten years at least 400 articles concerning cystic disease of the lung have appeared in the literature. Considered rare<sup>1</sup> twenty years ago, it is now a relatively common disease.<sup>2,3</sup>

Much of the past literature deals at length with the origin of pulmonary cysts. In the early literature the condition was considered to be congenital in origin, or at least the result of developmental arrest.<sup>1,2,4</sup> As the years passed, however, it became evident that in many cases the disease was acquired.<sup>5</sup> At present the literature gives the impression that cystic conditions of the lungs are probably more often acquired than congenital.<sup>6,7,8</sup> It is emphasized that the origin makes little difference, except for academic interest.<sup>9</sup> At one time it was thought that epithelization, particularly the stratified columnar type, indicated a congenital origin, now it is believed that in most cases such epithelium may occur in acquired cysts.<sup>9</sup> Because of destruction by infection, epithelium may be absent even in the congenital cysts,<sup>10</sup> therefore it is no longer a reliable criterion of origin. It is generally agreed that given a specific case of cystic disease of the lung, it is impossible to definitely determine whether its origin was congenital or acquired.<sup>11</sup>

Heretofore many names have been given to the condition<sup>4</sup> and at least twenty different terms appear in the literature.<sup>12</sup> Cystic disease of the lung has become the accepted term.<sup>11,13</sup> Thus, the congenital nature or the acquired nature of the origin is circumvented. The numerous individual descriptive names and the many classifications advanced<sup>2,4,11</sup> indicate the desire to segregate and describe different entities that may be cystic in nature. Since the general term, cystic disease of the lung, admittedly a hodgepodge of conditions, is gaining in favor, it would indicate a failure in the endeavor to separate the condition into different entities, it would also indicate the existence of some strong common denominator.

The literature indicates a fairly close agreement upon symptoms and classifies these in the following categories: (a) asymptomatic, (b) symptoms caused by increased pressure within the cyst, (c) symptoms caused by infection of the cyst, and (d) hemoptysis.

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Most patients with pulmonary cysts are in the asymptomatic group<sup>2 4 14 17</sup>

There is close agreement on the means of diagnosis by roentgenography, bronchography, bronchoscopy, and biopsy if open drainage is performed. In long-standing infection the roentgenogram reveals absence of retraction of the chest wall, lung or mediastinum, and absence of pleural thickening.<sup>3 12</sup> In uncomplicated cases the fluid-filled cyst may be confused with a neoplasm. The air and fluid containing cyst must be differentiated especially from pyogenic abscess and tuberculous cavities. The space containing only air offers less of a problem. However, if the cyst is large enough to fill the hemithorax, the differential point is the finding of lung parenchyma at the cardiophrenic angle and over the medial portion of the diaphragm. If biopsy of the cyst is possible it will reveal epithelium and, perhaps, bronchial structures.

There has been a wide variation in the accepted manner of treatment.<sup>4 15 16</sup> However, recent literature would indicate that extirpation is the procedure of choice and this may be accomplished by enucleation of the cyst, partial lobectomy, lobectomy, or pneumonectomy, depending upon the requirements of the individual case.<sup>4 11 18 19</sup> Infection may necessitate drainage preliminary to excision.

Since 1940 the author has treated fifteen patients with cystic disease of the lung. The range in ages was two months to fifty-six years. There were eight males and seven females. In seven instances the condition was present on the right side and in eight on the left side. The symptoms seemed to follow definite clinical patterns. In three patients the diagnosis was pyogenic lung abscess (Fig 1), two were treated for eighteen (Fig 1a and 1b) and twenty-four years (Fig 1c, 1d and 1e) respectively for chronic lung abscess. There were two cases of acute pyogenic pleural empyema and these were treated by open thoracotomy (Fig 2). Not until they were thought to be patients with chronic empyema was the true nature of the disease recognized. Two patients developed pleural empyema secondarily to the pulmonary cysts (Fig 3). Two developed cysts resulting from emphysema (Fig 4). One was an infant (Fig 4c, 4d and 4e), age two months, who followed a course as described by Caffey,<sup>20 21</sup> the other had an extremely large cyst that filled the left hemithorax (Fig 4b) displaced the heart to the right, and then herniated into the right pleural cavity. In two patients the cysts were associated with bronchiectasis (Fig 1e and Fig 5b and 5c). One case of cystic bronchiectasis was noted (Fig 5a). In one instance a cyst completely filled with fluid was diagnosed as carcinoma of the



FIGURE 1 Cystic Disease of the Lung Diagnosed as Chronic Lung Abscess

Fig 1 A and B, a white male, H D, age thirty-seven, had an open drainage of a lung abscess or empyema eighteen years before. He continued with symptoms of a mild form consisting of copious purulent expectoration, cough, and occasional episodes of fever. Findings characteristic of a lung cyst and trabeculations with an epithelial lining recently were found at open drainage. The presence of many bronchi opening into the cavity and a history of previous open drainage seem to indicate that it was an abscess cyst.

Fig 1 C, D and E, a thirty-three year old white woman, M G, developed

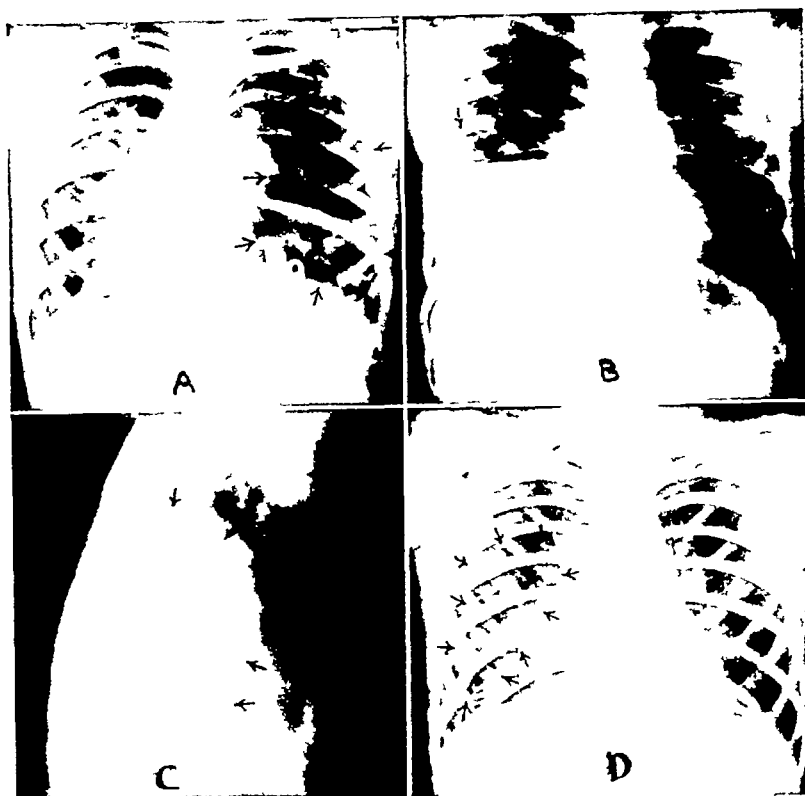


FIGURE 2 Cystic Disease of the Lung First Diagnosed as Acute Empyema and Later as Chronic Empyema

D H was a seven year old white girl. A diagnosis of generalized empyema was made and an open thoracotomy was performed. One year later the patient was referred for treatment of chronic empyema. Roentgenograms (Fig 2 A) revealed the absence of retraction of the chest wall and thoracic content and absence of pleural thickening. A biopsy led to a diagnosis of lung cyst. Lobectomy of the lower lobe of the right lung was followed by complete recovery.

Fig 2 B C and D was a nine year old white boy. F D Except for minor details his disease followed rather closely the same clinical course as D H. A lobectomy done elsewhere was successful.

A biopsy taken at the initial open drainage of the empyema would have made possible a correct diagnosis for both patients.

#### FIGURE 1—Continued

pulmonary symptoms at nine years of age following a tonsillectomy. An open thoracotomy was performed a few months after the onset. The wound healed but thereafter twice each day she would empty the lung of a large amount of purulent material. During her first pregnancy at the age of thirty-three severe pulmonary hemorrhages occurred. Because of associated bronchiectasis a pneumonectomy was done and the patient made an uneventful recovery. An epithelial lined cavity with trabeculations and many bronchi leading into it together with a history of a previous open drainage seem to indicate that it was an abscess cyst.

Fig 1 F a forty-two year old white male J N had a short period of illness. A diagnosis of pyogenic lung abscess was made. At open drainage the characteristics of an infected cyst were noted. Failure to heal was predicted, however healing was rapid and complete.



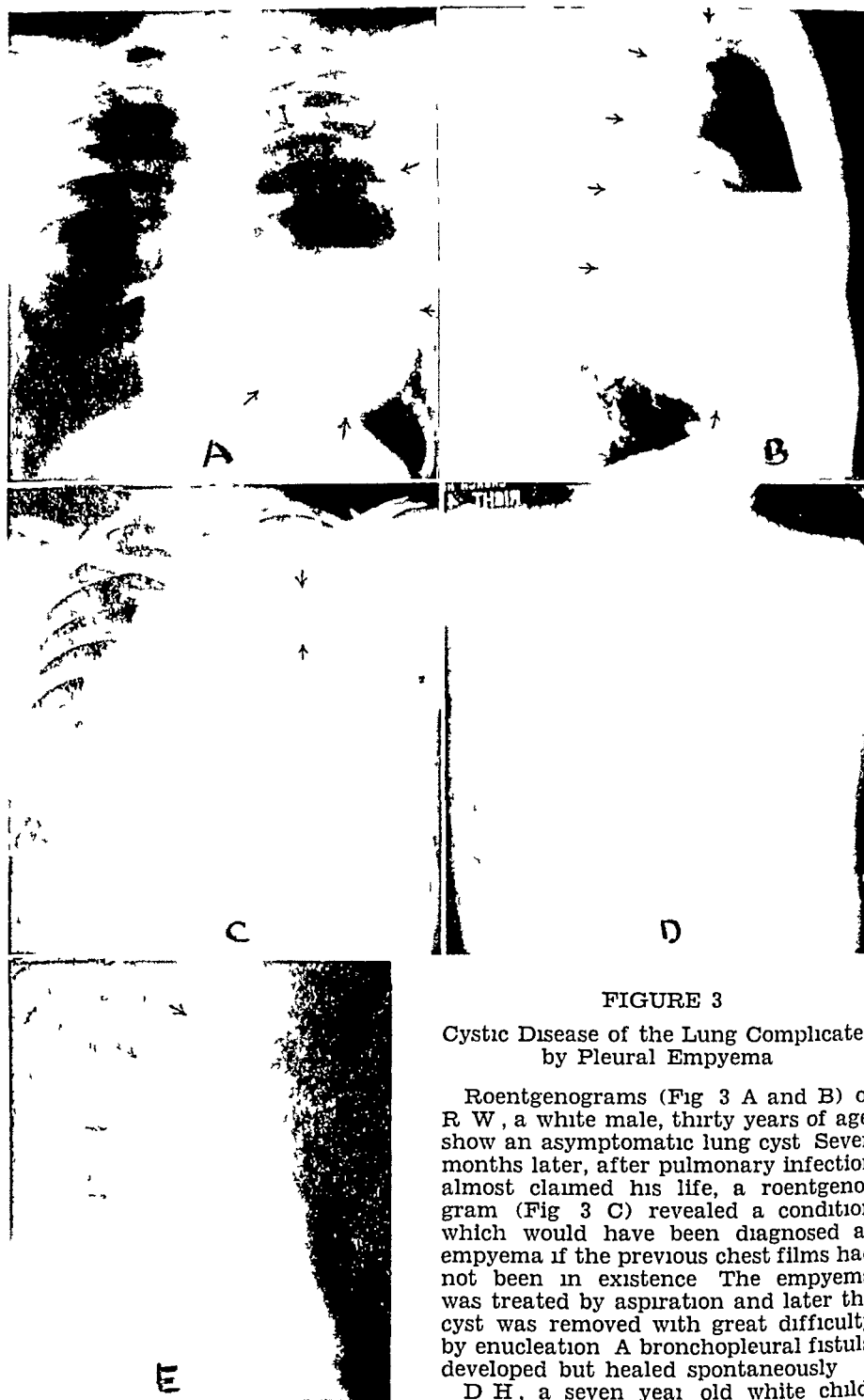


FIGURE 3

#### Cystic Disease of the Lung Complicated by Pleural Empyema

Roentgenograms (Fig 3 A and B) of R W, a white male, thirty years of age show an asymptomatic lung cyst. Seven months later, after pulmonary infection almost claimed his life, a roentgenogram (Fig 3 C) revealed a condition which would have been diagnosed as empyema if the previous chest films had not been in existence. The empyema was treated by aspiration and later the cyst was removed with great difficulty by enucleation. A bronchopleural fistula developed but healed spontaneously.

D H, a seven year old white child, was referred for treatment after open drainage of posterior empyema that was followed later by a thoracoplasty (Fig 3 D and E). The child was still extremely ill. The similarity of symptoms to those of R W led to the diagnosis of pulmonary cyst, formerly complicated by empyema. Open drainage anteriorly revealed characteristics of a lung cyst. Failure to heal was predicted but fortunately there was complete recovery.

lung before operation (Fig 6a and 6b) This patient was found to have a large systemic artery<sup>14 22</sup> supplying the cyst The remaining patients had uninfected (Fig 6) asymptomatic cysts, two of which were diagnosed during a period of severe pulmonary infection, probably secondary to the cysts The patient corresponding to Caffey's report required no specific treatment since the cyst disappeared spontaneously In two patients the cysts were healed completely by external drainage only Three were extirpated by enucleation One patient had a pneumonectomy because of bronchiectasis in the upper lobe whereas the cysts were in the lower lobe The remainder, or eight patients, were subjected to lobectomy There were no deaths, all have recovered completely and are asymptomatic

By a study of these patients certain conclusions seem evident Cystic disease of the lung is a rather common disease and, whether congenital or acquired, solitary or associated with some other disease, there is one common bond all have an epithelial lining Whether the cyst-like structure is congenital or acquired in origin as it develops from a minute size, it is always lined with a normal, healthy covering of epithelium Thus, there is no break in tissue continuity, the tissues are healthy and normal There is only a structural deformity It is important to realize that tissue destruction by infection does not initiate the development of the cystic condition, except in the externally drained pyogenic lung abscess If the origin of the cyst is closely associated with a bronchus it is lined with epithelium and there may be mucus glands or goblet cells In the event these glands or cells are present the cyst will have a fluid content unless emptied by a bronchus If the cyst arises in the manner of an emphysematous bulla it is associated with the alveoli whose walls are lined with flattened nucleated squamous epithelium<sup>23</sup> Therefore the cyst will be lined with flattened epithelium that is difficult to differentiate from mesothelium Accordingly, it will contain no mucus glands and will be air filled The cysts, moreover, will produce no symptoms until they become infected or develop abnormal intracystic pressure, either from air or fluid

Many times it has been reported that a lung abscess may become epithelial lined by the ingrowth of bronchial epithelium from communicating bronchi Incontestable proof of such an assumption has not been found by the author It must be accepted that such a condition might occur but only under ideal circumstances First, it would be necessary to have complete elimination of the infection and, accordingly, the cavity would obliterate before epithelization could occur Increased intracavitary pressure could prevent collapse of the cavity while epithelization takes place

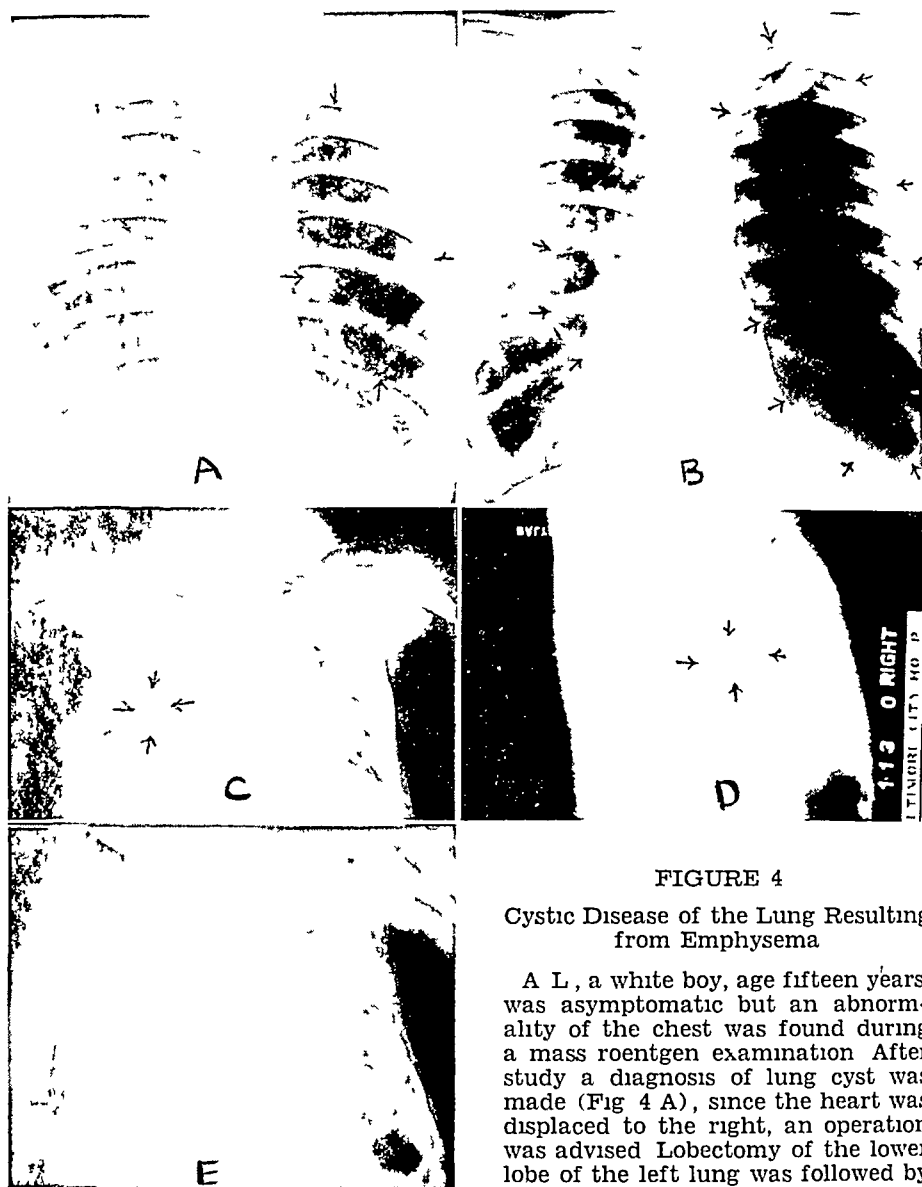


FIGURE 4

## Cystic Disease of the Lung Resulting from Emphysema

A L, a white boy, age fifteen years, was asymptomatic but an abnormality of the chest was found during a mass roentgen examination. After study a diagnosis of lung cyst was made (Fig 4 A), since the heart was displaced to the right, an operation was advised. Lobectomy of the lower lobe of the left lung was followed by recovery. The upper lobe of the left

was normal but the lower lobe showed considerable emphysema without a definite cyst.

C J was a white man, age forty-one years, with a gradual but progressive increase in dyspnea over a four year period. A diagnosis of spontaneous pneumothorax was made thirty months ago. During the past thirty months the cyst became enlarged by herniation into the right chest through the mediastinum (Fig 4 B). At operation the cyst wall was easily freed and was found to originate from the upper part of the upper lobe of the left lung. Several smaller areas of emphysematous bullae or cysts were present in the adjacent area. Excision of the cyst with the adjoining emphysematous bullae required the removal of only a small portion of the lung. The remainder of the lung appeared normal and expanded rapidly. The patient made an uneventful recovery.

R S, a white male, age two months, developed a pulmonary infection. A chest roentgenogram taken January 15, 1945 (Fig 4 C and D) is shown. The infant made a satisfactory recovery on appropriate medication and a roentgenogram taken January 31, 1945 (Fig 4 E) revealed no evidence of the cavity or cyst. The last roentgenogram of the chest was taken March 14, 1945 and the cavity had not

Such pressure would indicate incomplete drainage, therefore, infection could not be overcome and epithelization could not take place. In considering the incidence of pyogenic lung abscess there would be a great many more epithelial lined spaces encountered if epithelization were actually a step in the pathogenesis of pyogenic lung abscess. Many authors have opposed this point of view.<sup>9 10 24</sup> The lattice lung described as an epithelized lung abscess is strikingly similar to the one described as an infected lung cyst.<sup>9 24 25</sup> Thus the question arises as to whether they may not be one and the same condition. Patients with infected pul-

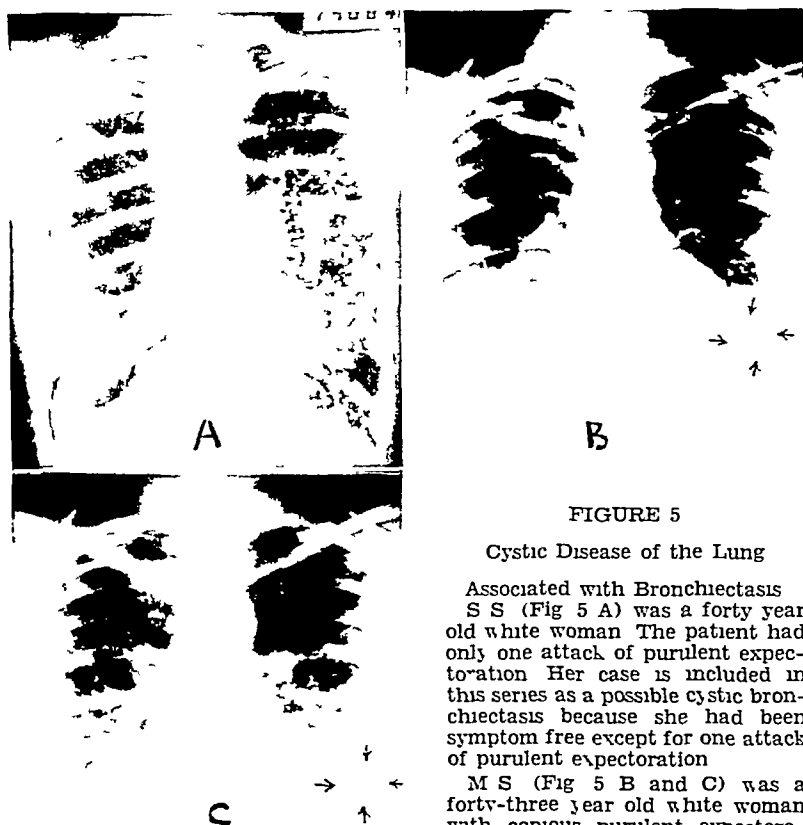


FIGURE 5

## Cystic Disease of the Lung

## Associated with Bronchiectasis

S S (Fig 5 A) was a forty year old white woman. The patient had only one attack of purulent expectoration. Her case is included in this series as a possible cystic bronchiectasis because she had been symptom free except for one attack of purulent expectoration.

M S (Fig 5 B and C) was a forty-three year old white woman with copious purulent expectoration. Lobectomy of the lower lobe

of the left lung was followed by recovery.

M S (Fig 5 B and C) and M G (Fig 5 C D and E) are probably patients with bronchiectasis secondary to or merely associated with pulmonary cysts.

## FIGURE 4—Continued

reappeared. This patient represents the condition termed regional obstructive emphysema described by Caffey.

It appears likely that this group of cysts was emphysematous in origin. A L did not have a lung cyst but his roentgenogram is shown since perhaps it is a stage in the development of an emphysematous type of lung cyst.

monary cysts diagnosed as lung abscess have a mild course when compared with the course of a true pyogenic lung abscess, and the chest roentgenograms fail to reveal retraction of the chest and thickened pleura. Of course, when the infected lung cyst is drained it usually will not heal because of the epithelial lining. The origin of pyogenic lung abscess by suppurative tissue destruction would definitely set it apart from an infected pulmonary cyst.

If a pyogenic abscess of the lung is drained externally a condi-

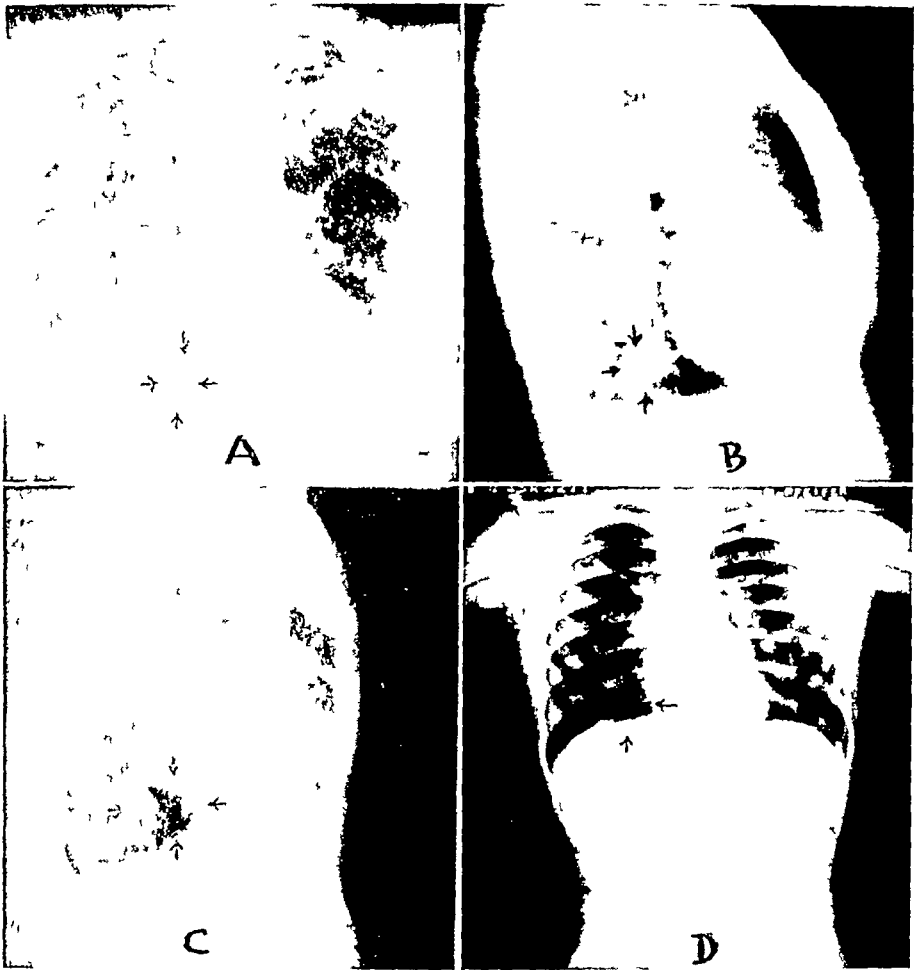


FIGURE 6 Cystic Disease of the Lung, Asymptomatic and Uncomplicated

M A (Fig 6 A and B) was a fifty-six year old white woman who expectorated blood on only one occasion. Carcinoma of the lung was the preoperative diagnosis. Lobectomy of the lower lobe of the right lung was followed by recovery. A large, pencil size systemic artery entered the lung at the region of the cyst.

N P (Fig 6 C and D) a five year old white girl, had no symptoms. Lobectomy of the lower lobe of the right lung was followed by recovery. It is interesting to note that the cyst is the third of the series that contained only air. This cyst was within the lung parenchyma instead of on the surface as represented by C J (Fig 4 B). The cyst in this patient first was found at the time of a pulmonary infection but after many months' observation it did not disappear as in R S (Fig 4 C, D and E).

tion suitable for epithelization is produced. The infection is overcome and, if for any reason the space does not collapse, epithelium from the communicating bronchi can grow into and cover the walls of the space. This view is held by Edwards<sup>25</sup>. The epithelized space continues to drain because of the presence of mucus glands and goblet cells in the lining membrane. Bronchial communication is usually free and if the external wound is allowed to heal there results the equivalent of an epithelized cyst. When more

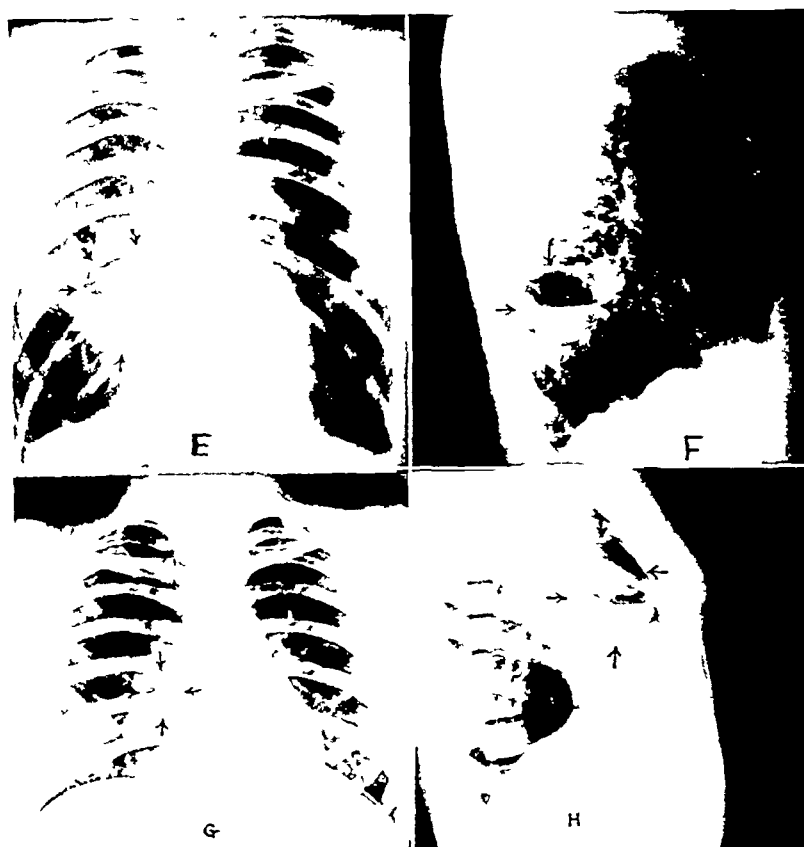


FIGURE 6 (Continued) Cystic Disease of the Lung  
Asymptomatic and Uncomplicated

J. R. (Fig. 6 E and F) was a twenty-two year old white man who had a roentgenogram of the chest following a pulmonary infection three months before. He remained free of symptoms. Lobectomy of the lower lobe of the right lung was followed by recovery.

J. W. (Fig. 6 H and G) a thirteen year old white girl had a course similar to J. R. The cyst was enucleated with recovery.

These four patients represented three types of cysts: one completely filled with fluid, one completely filled with air, and two with both air and fluid. These cysts are probably congenital in origin.

than one bronchus communicates with an epithelized space it seems reasonable to expect that the space is an old epithelized lung abscess. Two of the cases (Fig 1a, 1b and Fig 1c, 1d, 1e) herein reported undoubtedly represent epithelized cavities occurring after drainage of a lung abscess. Both patients presented trabeculation within the cavity and both had many bronchi leading into the epithelized cavity. The history of external drainage shortly after the onset of the disease sets them apart as instances of epithelized lung abscess.

The healing of tuberculous cavities by epithelization has been described<sup>26 28</sup>. If healing by epithelization were a step in the pathogenesis of tuberculosis there would be on record many examples, since tuberculosis with cavitation is a common disease. One can assume that such cases as are described might easily have been lung cysts and that pulmonary tuberculosis was coincidental. Many cases of cystic disease of the lung have been diagnosed incorrectly as tuberculosis<sup>1 3</sup>.

Since the pulmonary cysts in cystic lung disease are not initiated by infectious tissue destruction, the onset is insidious and silent. From their inception the cysts are lined with a healthy epithelium. Therefore, they are resistant to infection because there is no portal of entry. The usual absence of pleural infection when air escapes from healthy parenchyma of the lung into the pleural cavity would indicate that regardless of the type of bacteria present in the upper respiratory passages, the lower portions of the lung are normally free of bacteria. The pulmonary cysts are generally connected with bronchioles or respiratory bronchioles, or even alveoli, and therefore, they are seldom exposed to infection. When infection does occur it is usually rather mild because of the resistance and limiting effect of the lining membrane.

It is difficult to associate bronchiectasis with cystic disease of the lung. However, a cystic type of bronchiectasis does occur and sometimes the cysts are large<sup>3</sup>. It can be assumed that epithelial lined dilations occur without tissue destruction by infection and often remain asymptomatic. Because of the lining membrane the course of an infected cystic bronchiectasis is mild compared to bronchiectasis that develops by actual tissue destruction. One patient in the series (Fig 5a) probably represents cystic bronchiectasis. Her only symptoms occurred during a short period of secondary infection. The patients shown in Fig 5b, 5c and Fig 1c, 1d, 1e probably represent bronchiectasis associated with or secondary to cystic disease of the lung.

The mechanism of the development of the cyst-like structures from emphysematous bullae and the mechanism for development of subsequent pressure symptoms have been described adequately.

ly<sup>29 30</sup> It is important to point out that the condition occurs in adults as well as in infants or children

† In the two patients who recovered completely after simple open drainage it can be argued that they did not have infected lung cysts. However, both had epithelial lined cavities and typical trabeculations much like the lattice lung. Neither patient had a previous external drainage. One can assume that destruction of the lining membrane was so complete that healing ensued. Failure to heal was predicted for both.

In a discussion of cystic disease of the lung, the cysts of the pleura and mediastinum should be excluded and most authors also omit the echinococcus cysts.<sup>2 31</sup> The classification of Dickson, Clagget and MacDonald<sup>11</sup> with minor modifications seem highly satisfactory.

- I The true developmental or so-called congenital cysts of the lungs (some of the bronchogenic cysts or bronchoalveolar cysts)
- II Acquired cysts or cyst-like cavities of the lungs
  - A Cystic bronchiectasis
  - B Other pulmonary cysts or cyst-like cavities
    - 1 Emphysematous bullae
    - 2 Obstructive emphysematous cyst of Caffey
    - 3 Abscess cysts (after external drainage)
    - 4 All other pulmonary cysts

The obstructive emphysematous cyst described by Caffey and represented by Fig 4c, 4d and 4e should have a prominent place in any classification since the condition is distinctive. It occurs only in infants and it regresses to complete obliteration on appropriate medication for pulmonary infection. Spontaneous obliteration has not occurred in infants over one year of age.

Extirpation of the cyst is the treatment of choice. The method of extirpation depends upon the location of the cyst. If it is placed peripherally to the lung parenchyma, it can be enucleated or removed by partial lobectomy. If the cyst is completely surrounded by lung parenchyma, lobectomy is the procedure of choice. The only pneumonectomy performed in the present series was made necessary by the cysts involving the lower lobe of the lung and the upper lobe of the lung was involved extensively by bronchiectasis. Severe infection may make preliminary drainage of the cyst imperative. When open drainage of the pleural cavity or pulmonary suppurative condition is accomplished a biopsy should be made. It may lead to the correct diagnosis of the condition.



## CONCLUSIONS

- 1) An epithelial lining membrane is the common characteristic that binds together the apparently diversified conditions included under the term "Cystic disease of the lung"
- 2) As a result of the epithelial lining membrane the pulmonary cyst, whether congenital or acquired, presents definite symptom patterns, and runs a mild course when infected
- 3) Because pulmonary cysts have an epithelial lining membrane, extirpation is the treatment of choice

## CONCLUSIONES

- 1) La característica comun a todos los estados aparentemente diversos que se incluyen bajo el término de "Enfermedad Quística del Pulmón" es que tienen una membrana epitelial
- 2) Por razón de la membrana epitelial el quiste pulmonar, ya sea congénito o adquirido, presenta complejos sintomaticos bien definidos, y evoluciona levemente cuando esta infectado
- 3) Debido a que los quistes pulmonares tienen una membrana epitelial, la extirpacion quirurgica es el tratamiento de elección

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## D I S C U S S I O N

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Dr Brantigan is to be congratulated for his excellent paper which represents an exhaustive analysis of numerous articles which have appeared particularly during the past few years, and is the result of a large and successful experience in the surgical management of cystic disease of the lung, which permits certain definitive conclusions. As an internist, there is little that I can add, indeed, my few cases were treated surgically by him. One, a simple asymptomatic cyst which was discovered accidentally. Another, also discovered accidentally, proved to be a large emphysematous area. At the time of operation, this patient presented something of a problem regarding what to do. Dr Brantigan decided to remove the involved lobe, and the heart, which had been somewhat displaced, returned to normal position. After operation, the case was considered carefully, and it was decided, particularly by Dr Brantigan, that in similar instance, surgical removal would be indicated. The third case we both felt was an

acute lung abscess, at operation it was found to be an infected cyst, which was appropriately drained with the idea of follow-up surgery at a later date. Interestingly enough, the wound has completely healed, the man is perfectly well, and his last roentgenogram is negative.

While cystic disease of the lung is by no means rare, one may wonder whether we are justified in referring to it as "common." Dr. Brantigan has certainly seen a large number during the past seven years, however, we must realize that these cases are, to use his words, channeled to him as a thoracic surgeon practicing in a large city.

As regards diagnosis, this does not present too much difficulty as a rule, however, there are instances, as noted previously, in which the true nature of the process may be missed. If full of fluid, the matter of a tumor, let alone abscess, empyema, aneurysm and dermoid cyst, must be ruled out.

Dr. Brantigan reports one instance in which an unusual vessel was encountered, this calls to mind that cystic disease of the lung has not infrequently been associated with various pulmonary anomalies, such as accessory lobes and aberrant vessels, the latter should particularly be kept in mind at operation.

The rapid strides in thoracic surgery during the past ten years have made the surgical removal, by one or the other of the methods enumerated by Dr. Brantigan, an almost universally accepted procedure. The patients presenting symptoms as a result of cystic disease, either simple or complicated, certainly should be subjected to surgery, unless some particular contraindication be present, these need no comment. It has been repeatedly stated that uncomplicated cystic pulmonary lesions must be uncommon, this in a measure is substantiated by the infrequency of the lesion at the autopsy table, and in the course of the mass x-ray surveys being conducted throughout the country. One cannot help but be impressed with the relative benignity of the complicated cystic disease, this is amply demonstrated by Dr. Brantigan's cases and those appearing in the literature. Realizing the infrequency of the simple cystic disease without symptoms, there is probably no point in arguing against the advisability of surgery in these instances. In culling the literature, one is impressed by the fact that most articles have been written by surgeons or roentgenologists. With these facts in mind, would it be too far off the beaten path to suggest expectant treatment, with frequent roentgen studies, in the uncomplicated, asymptomatic cases in which the cyst is not too large?

Dr. Hudson called attention to the possibility of malignancy developing in cysts of the lung. I had not been impressed by this

possibility and, if proven, would, of course, preclude any expectant therapy

Cystic disease of the lung, first recognized about two hundred and fifty years ago, made its real debut as a supposedly congenital condition in Dr Koontz's paper in 1925. As alluded to in Dr Brantigan's paper, the pendulum has swung well toward the side of the condition often being acquired. The disease has now come of age, it has achieved an important place in chest diseases and deserves our careful consideration

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## D I S C U S S I O N

WILLIAM A HUDSON, M.D

Detroit, Michigan

Dr Brantigan very wisely reviews the different theories concerning the origin of pulmonary cysts. It would seem proper to use the term Cystic Disease of the Lungs to include all cyst-like conditions which cannot be definitely associated with some indisputable cause or origin until such a time as we shall find some indisputable evidence by which we can differentiate the acquired from the congenital cysts of the lung.

He wisely points out the value to clinical history and clinical findings when considered together with proper laboratory procedures in the diagnosis of such conditions. The treatment is, for the most part, surgical.

I reported a case of acquired cyst of the lung at the Meeting of the Southern Chapter, of the American College of Chest Physicians in 1946, showing photographic records of the cyst with the inner wall of the cyst being formed by denuded lung, the outer wall formed by visceral pleura. This cyst-like structure had apparently been produced as a result of a sudden compression of the chest in an automobile accident several months previously. There were x-ray films available to support this contention.

May I congratulate Doctor Brantigan on his fine presentation.

# The Problem of Bronchiectasis\*

## A Review

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Bronchiectasis, like pulmonary tuberculosis, is a killer of men, but bronchiectasis, unlike tuberculosis, kills on a fairly definite schedule Tuberculosis, unless in a terminal state, tends to heal if given a chance, and we see many people who once had far advanced active pulmonary tuberculosis, who have regained a measure of health and economic independence, but we see very few bronchiectatic patients with far advanced disease who are ever able to do more than live a miserable, dependent existence, the tendency of bronchiectasis is to progress downward Head<sup>1</sup> found, in a group of two hundred bronchiectatic patients, who had acquired their disease in the first ten years of life, that few were living after forty years of age Riggins,<sup>2</sup> from observations at the Bellevue and Lennox Hill Hospitals, New York City, agreed with Head for the most part, but also saw a fair sprinkling of bronchiectatic patients in their sixth or seventh decades While Roles and Todd<sup>3</sup> observed a forty-seven per cent mortality in forty-nine non-surgically treated patients that were followed for six years Clagett and Deterling, Jr,<sup>4</sup> stated that some bronchiectasis was found in two per cent of all the necropsied cases at the Mayo Clinic

The bronchiectasis found in the right upper lobe and in the upper portion of the left upper lobe due to atelectasis, bronchial stenosis, and contracting scar tissue and following various inflammatory conditions of the lung (including tuberculosis), is relatively benign because the drainage is downhill, the drainage of bronchiectatic lesions in the lower lobes, right middle lobe, and lingula of the left upper lobe is uphill, and more liable to pursue a progressive course Also, there may be a more or less temporary bronchiectasis following acute respiratory infections as bronchitis, virus pneumonia, and which follows enlarged hilar glands as from primary phase tuberculosis, in these cases the bronchiectasis follows bronchial stenosis with its tendency to trap inspired air and prevent its egress, combined with areas of atelectasis which increase the negative pull of the pleural space, this type of bronchiectasis has a tendency toward recovery when the

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\*Read before the Glendale Branch of The Los Angeles County Medical Association, at Glendale, California, October 20, 1947

causative conditions are removed, provided the bronchial walls do not become grossly infected

Bronchiectasis, as we ordinarily understand it, is an acquired dilatation of the bronchi and bronchioles and the primary lobules or lung units of the pulmonary parenchyma. But before going further into the etiology, pathogenesis, pathology, and treatment of bronchiectasis, it seems advisable to briefly review the developmental and final anatomy of the tracheo-bronchial tree and lungs in order that these phases may be better understood.

The anlage of the larynx, trachea, bronchi, and lungs arises about the fifteenth day (embryo of 23 segments, 3.2 mm in length) from an outgrowth in the ventral wall of the entodermal tube (the foregut, the primitive oesophagus). This anlage is known as the laryngotracheal groove. The caudal end of this outgrowth promptly becomes rounded and marks the future development of the bronchi and lungs, constriction of the groove proceeds cephalad and it becomes separated from the primitive oesophagus, the cephalic portion becoming the larynx and the intermediate part becoming the trachea<sup>5,6</sup>. The rounded, caudad portion, the lung bud, becomes bilobed in four to five millimeter embryos. Both lung buds elongate, the right being slightly larger than the left at first. These lung buds (stem buds, main bronchial stems) grow downward, lateralward and backward, branching monopodially to give rise to the future bronchi. In the later stages of development there is probably dichotomous branching of the smaller bronchi<sup>5,6</sup>.

In the seven millimeter embryo, from the stem bronchi, two bronchial buds arise on the right side (the apical bud, future right upper lobe bronchus, and a ventral bud, the future right middle lobe bronchus), a ventral bud also arises on the left bronchus (the future left upper lobe bronchus), the main bronchial stems or buds become the lower lobe bronchi<sup>5,6</sup>. These future bronchi grow into a mass of mesenchymal cells and carrying before them folds of mesoderm. The mesenchyme forms the cartilage plates, muscle, connective tissue of the lungs, and tracheal and bronchial walls. Blood vessels and nerves grow into this developing mass. The visceral (splanchnic) mesoderm forms the visceral pleura, and the somatic (parietal) mesoderm forms the parietal pleura. The entoderm of the primitive trachea and bronchi forms the epithelium lining of these and the lining of the lung units<sup>5,6</sup>. The air cells or alveoli begin to form at about the sixth month, and the lung is fully formed when birth takes place<sup>5,6</sup>.

Macklin<sup>7</sup> considers the tracheo-bronchial tree as far as the respiratory bronchiole, as merely a conduit system, while the

part beginning with the respiratory bronchiole and ending with the pulmonary alveoli is the functional part. The bronchi, when they enter the lungs, become cylindrical and gradually acquire a circular layer of smooth muscle on the outer border of the tunica propria. These muscle fibers become more and more prominent as the smaller bronchi are reached, and are found to extend as far as the atria.<sup>6</sup> The other elements of the bronchial wall (cartilage, white fibrous tissue, elastic tissue, glands, etc.) decrease as the smaller bronchi are reached. The circular muscle is best developed in the terminal bronchiole, and can exert a strong sphincteric action in bronchospasm,<sup>8</sup> as the bronchi grow smaller, the cartilagenous rings change to small plates or flakes, and disappear in bronchi of about one millimeter diameter.<sup>6</sup> The mucus glands also disappear about here<sup>6</sup> (Fig 1).

Stratified, ciliated, columnar epithelium lines the trachea and larger bronchi, as the bronchi grow smaller, this becomes simple, columnar, ciliated epithelium, then ciliated cuboidal epithelium, when the respiratory bronchiole is reached, the epithelium becomes simple cuboidal with areas of squamous or respiratory epithelium. The remaining portion of the tract (alveoli, air cells) are lined with squamous epithelium, probably deficient<sup>8</sup> in places (Fig 2).

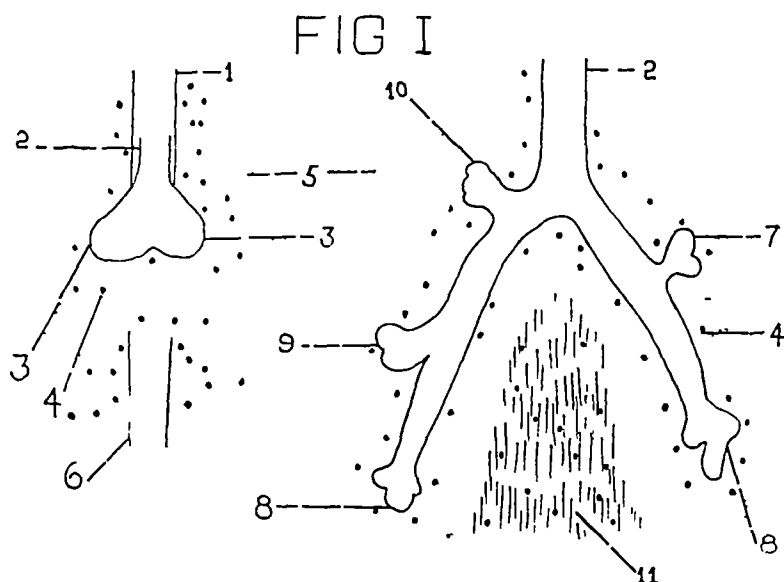


Diagram of origin of lungs and bronchi

1, Entodermal tube (fore-gut), 2, primitive trachea 3 lung bud from ventral aspect of entodermal tube, 4, mesenchyme, 5, mesothelium (visceral), future visceral pleura, 6, primitive esophagus from fore-gut, 7, ventral bud (future left upper lobe bronchus), 8, stem buds (main bronchial stems), 9, ventral bud (future middle lobe bronchus), 10, apical bud (future right upper lobe bronchus) On left side, apical bud in ventral bud, no separate lobe on left side comparable to right upper lobe, 11, septum transversum (future diaphragm)

Miller's<sup>12</sup> lung unit begins with the respiratory bronchiole (bronchiolus respiratorius) which gives off several alveolar ducts (ductuli alveolaris, alveolar passages, vestibules), each alveolar duct gives rise to several irregularly spherical dilated parts, the atria, each atrium originates several alveolar sacs (sacculi alveolaris, infundibula, air sacs), and in each alveolar sac wall, there arise a number of alveoli (alveoli pulmonis, air cells) Best and Taylor's<sup>5</sup> description of a lung unit or primary lobule begins with the respiratory bronchiole, which is a continuation of the terminal bronchiole, and has the same length (0.2-0.5 mm) and diameter (0.3-0.4 mm), five or six alveolar ducts arise from one respiratory bronchiole, and an alveolar duct gives origin to three to six alveolar sacs after a variable number of rebranchings, an alveolar sac contains a number of small pouches, the alveoli. As the bronchioles approach the periphery of the lung, they grow shorter, but maintain about the same diameter as the earlier ones (0.3-0.4 mm), the first branches being about 15 millimeters in length.<sup>8</sup>

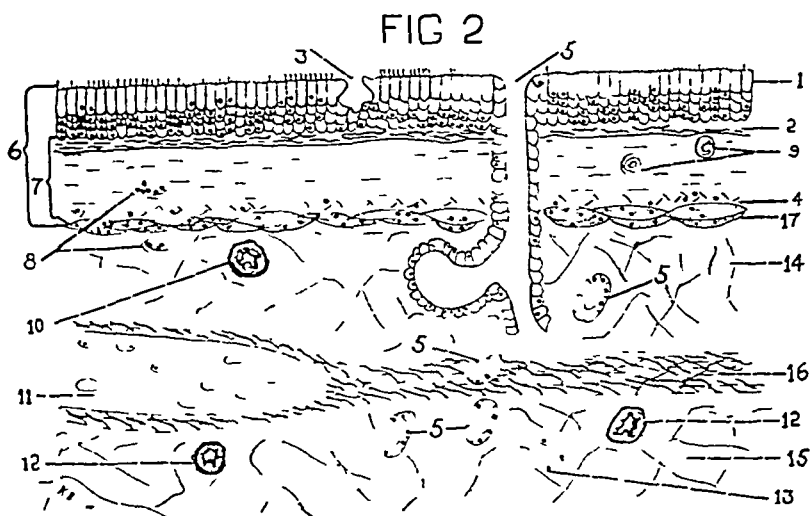


Diagram of cross section of medium-sized intrapulmonary bronchus

1 Stratified ciliated columnar epithelium 2 basement membrane (membrana propria) 3 goblet mucus cell 4 outer layer of tunica propria shows longitudinal elastic fibers cut across and white fibrous tissue inner layer shows fine loose fibers and basement membrane 5 racemose mucus and serous gland opening on mucus surface and extending into adventitia 6 mucus membrane 7 tunica propria (corium) 8 lymph gland 9 10 12 blood vessels All layers contain blood vessels nerves lymphatics and secreting glands 11 hyaline cartilage plate in dense fibro-elastic layer 13 fat cells 14 submucosa of coarse loose areolar tissue with glands vessels nerves and lymphatics 15 adventitia of loose areolar tissue with glands vessels nerves and lymphatics 16 fibro-elastic layer of white fibrous tissue and yellow elastic fibers densely arranged 17 circular smooth muscle layer in mucus membrane



The essential etiology and pathogenesis of bronchiectasis can be summed up in a few words. Stenosis of a bronchus with retained infective secretions permit infection of the bronchial walls, with weakening of such stromal elements as elastic tissue and muscle, and permit the rythmical pull of inspiration, possibly combined with the weight of the pooled secretions, gradually to dilate the walls of the bronchi and lung units into permanent or potential cavities. When there is atelectasis of portions of the surrounding lung, or when there is contracting, inelastic, fibrous tissue in the surrounding lung, this inspiratory pull is greatly increased, when there are also partly occluded bronchi which permit air to enter, but which exert Chevalier Jackson's well known check-valve action in preventing egress of some of the air, the dilating effect on the infection-weakened walls is heightened.

The bronchiectasis, mainly in the upper lobes, caused by the irregularly developing fibrosis of chronic tuberculosis produces dilatation in the distorted, gnarled bronchi which does not present the regular pattern seen in ordinary lower lobe bronchiectasis with its more evenly developing fibrosis.<sup>13</sup> Even so, this upper lobe bronchiectasis of tuberculous fibrosis is usually relatively benign because the drainage is downhill, but the bronchiectasis that follows invasion of the bronchial walls by tubercle bacilli, with possible secondary infection by ordinary pyogenic bacteria, is one of the severe complications of pulmonary tuberculosis, and may require surgical removal.

Bronchiectasis can develop at any age, but a large percentage of cases develop during the first ten years of life. Perry and King<sup>14</sup> claimed that the onset of 42 per cent of their patients was during the first ten years, and that the onset occurred in 27 per cent during the second ten years. Farrell<sup>15</sup> stated that 80 per cent of his bronchiectatic patients acquired their disease during the first ten years.

Singer and Graham<sup>16</sup> pointed out that the dense, triangular shadows seen along the mediastinal borders with bases on the diaphragmatic leaflets, apices in the hill, and hypotenuses facing peripherally were due to atelectasis of lower lobes. These are seen principally in infants and young children. There are similar, but larger and less dense triangular shadows which are due to interstitial infiltration and fibrosis in bronchiectasis.

McNeil, MacGregor and Alexander,<sup>17</sup> Richards,<sup>18</sup> and Anspach,<sup>19</sup> showed that these triangular areas of atelectasis frequently accompanying pneumonia, were often followed by bronchiectasis later, especially in infants and children. The smaller bronchi of infants and children are especially susceptible to plugging, from thick, tenacious secretions with attendant atelectasis. It is a law

of the cube that the smaller bronchi would present a relatively greater surface for adherence per unit of volume than the larger bronchi

Anything which causes bronchial stenosis predisposes to bronchiectasis. The inflamed bronchi of whooping cough, measles, bronchopneumonia, and bronchitis, are special sources in childhood, enlarged tracheobronchial and hilar glands following acute and chronic infections, and tuberculous adenitis of these glands may cause stenosis of the bronchi with development of bronchiectasis. The inhalation of foreign bodies with the drowned lung beyond the obstruction are frequent sources of bronchiectasis, particularly in children, and as Chevalier Jackson pointed out long ago, the vegetable body as the peanut is more liable to encourage bronchial and pulmonary suppuration than the metallic one.

There is a form of chronic bronchitis and bronchiectasis occurring in children having cystic fibrosis of the pancreas. The lack of exocrine secretion of the pancreas with failure to digest fats and other nutritional constituents causes lack of absorption of vitamins A and D and malnutrition, these in turn permit infection of the respiratory tract with pyogenic organisms, espec-

FIG 3

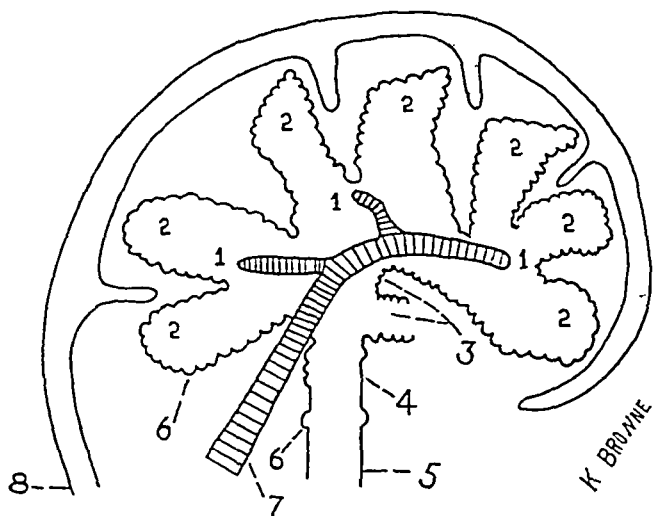


Diagram depicting William S. Miller's primary lobule or lung unit

1 atria 2 alveolar sacs (infundibuli) 3 alveolar ducts (vestibuli)  
 4 respiratory bronchiole 5 terminal bronchiole 6 alveoli (air-cells)  
 7 pulmonary arteriole accompanying terminal bronchiole and giving  
 a branch to each atrium then forming capillary plexuses around  
 alveoli 8 pulmonary venule collecting from plexuses then following  
 partly independent course back to heart but joining other venules

ially staphylococci, as with other vitamin A deficiencies, there is a piling up of epithelial debris in the salivary gland ducts, trachea and bronchi

Kartagener<sup>20</sup> found bronchiectasis and sinusitis frequently associated with dextrocardia and situs inversus, the "Kartagener triad" He cited this in support of the theory that bronchiectasis is congenital Adams and Churchill<sup>21</sup> reported five cases of this syndrome Olsen<sup>22</sup> reviewed 85 cases of dextrocardia seen at the Mayo Clinic from 1920 to 1941, inclusive, evidence of bronchiectasis was found in 16.5 per cent of these cases in contrast to less than 1 per cent of bronchiectasis in all other patients registered there He also mentioned bronchiectasis occurring in pairs of identical twins as further evidence for the congenital theory of bronchiectasis

Any condition of the lungs and bronchi that causes fibrosis or bronchial stenosis or both as pneumoconiosis, corrosive gases, fungus infections, bronchopneumonia, bronchitis, pleural empyema, lung abscess and the like, may be causative of bronchiectasis Benign or malignant intrabronchial tumors, extrabronchial tumors, large glands, or fibrotic bands pressing on the bronchial walls all encourage the development of bronchiectasis Uncomplicated pneumococcus lobar pneumonia rarely causes bronchiectasis, because the involvement here is primarily parenchymal and not bronchial But the virus types of pneumonia are frequently followed by the development of bronchiectasis Here, there is an intense inflammatory involvement of the bronchial and peribronchial tissues as well as an alveolar exudate and hemorrhagic pneumonitis The partly occluded bronchi with their damaged walls and retained infective secretions, the scattered areas of atelectasis all favor the invasion of secondary bacterial pathogens into the bronchial walls and surrounding tissues

Watson and Kibler<sup>23</sup> reiterated an earlier theory of theirs that allergy of the bronchial tubes with its attendant bronchial stenosis and retention of secretions was the most frequent cause of bronchiectasis It is true that the bronchial swelling and muscle spasm of allergy furnish a good foundation for the development of bronchiectasis, but is not the only mechanism that does so

The pathological changes in bronchiectasis are varied The invasion of the bronchial walls and surrounding lung tissue by the pathogenic bacteria and defence white cells of the blood is followed by varying degrees of destruction and replacement by inelastic, white fibrous scar tissue The scar tissue, when young and gelatinous, is easily stretched by inspiration and the weight of retained secretions, but becomes hard and contracted when older There is loss of the elastic elements in the bronchial walls

The ciliated, columnar epithelium may be eroded in places, leaving granulation or scar tissue in its place, or it may be replaced by flattened epithelium devoid of a ciliary fringe with its self cleaning action. Blocked, infected secretions may extend into the lung, producing lung abscess or pleural empyema.

After each bout with an acute respiratory infection, the chronic bacterial infection spreads more extensively into the bronchial walls and lung parenchyma, leaving more destruction and scar tissue formation. A greater and greater load is added to the right side of the heart by the mechanical obstruction to blood flow and the replacement of functional units in the lung. This recurs until the right ventricle fails and eventually congestive heart failure develops. This heart failure responds to cardiac treatment for a time, but if the patient does not die subsequently of metastatic abscess, pneumonia amyloid disease, nephritis, or massive hemorrhage, he will eventually die of heart failure from the chronic overwork, and infectious or toxic myocarditis from the pulmonary infection.

The left lower lobe is the one most frequently involved in bronchiectasis, and when bronchiectasis develops here, the lingular segment of the left upper lobe frequently becomes affected. Churchill and Belsey<sup>24</sup> found the lingular segment sufficiently involved to require surgical removal in eighty per cent of cases requiring removal of the left lower lobe. This frequent left sided localization is probably mainly a matter of drainage, the left main bronchus and its branches make more of an angle with the trachea than does the right one, which is more of a continuation of the trachea. Clagett and Deterling<sup>4</sup> found the following lobar distribution in 471 bronchiectatic patients seen at the Mayo Clinic: the right lower lobe in 19 per cent, the left lower lobe in 35 per cent, both lower lobes in 19 per cent, the right middle lobe seldom. While these statistics agree fairly with those of others, there are a considerable number of patients who have right middle lobe bronchiectasis accompanying bronchiectasis of the right lower lobe.

There is no micro-organism distinctive of bronchiectasis, but streptococci (including viridans or alpha type, hemolyticus or beta type non hemolyticus or gamma type and probably some anerobic types) seem to play an especially prominent role in bronchiectasis. The pathogenic significance of streptococcus viridans is not yet settled. *Monilia albicans* is found occasionally as a secondary saprophytic invader but may possibly at times assume pathogenic importance. The fusiform-spirilla group is only rarely found in bronchiectasis, and then mainly as a saprophytic invader. The bad odor found in the sputum of some bronchiectatic patients

is now thought to be rarely caused by this group. This odor is now attributed by many, to other organisms, as the anaerobic streptococcus. The *Neisseria catarrhalis* is considered by many to play little or no part in the disease process.

In some quarters, there is a marked swing away from the former tenet that sinusitis is a cause of bronchiectasis, and some present day observers even claim that the sinusitis present is caused by the bronchiectasis. I have found that sinusitis is very frequently associated with bronchiectasis, and that very little permanent result can be secured by either medical or surgical treatment in bronchiectasis if the accompanying sinusitis cannot be controlled, and very often a case of early bronchiectasis can be improved by merely clearing up the sinusitis present. The protagonists of the sinusitis etiology of bronchiectasis postulate two possible routes of spread of infection to the bronchi: the inhalation route, and the lymphatic route, the former having the most supporters.

The diagnosis of advanced bronchiectasis is usually easy, the coughing up of large amounts of purulent sputum, the dyspnoea and cyanosis, the clubbed fingers, the low grade temperature with acute exacerbations, the history of frequent pneumonia like attacks, especially during the cold months, the hemoptysis varying from slight streaking, to massive pulmonary hemorrhage, all give definite leads to the diagnosis. There is present at some time, a myofascitis, especially along the paravertebral muscles, and often segmental neuralgia, frank rheumatoid arthritis is also seen, but less often.

To diagnose early bronchiectasis, or the prebronchiectatic state, constant diagnostic suspicion and readiness to act are necessary, what seems to be unresolved pneumonia may be an atelectatic lobe with bronchiectasis developing, the subacute sinusitis, or bronchitis, may already be complicated by early bronchiectasis, the persistent low grade temperature, weight loss, and listlessness, with or without marked cough, that hangs on after an acute respiratory infection, may be the first vague hint of developing bronchiectasis. In any suspected case, bronchography should be done. If there is any suspicion of atelectasis from a mucus plug, growth, or pressure from outside the bronchus, a bronchoscopy should be done.

The treatment of advanced bronchiectasis is surgical removal of the affected areas if this can still be done, lobectomy, lingulectomy and other segmental operations, or even pneumonectomy occasionally are the surgical methods in use. The operation of lobectomy twenty-five years ago, carried a mortality rate of about 50 to 60 per cent, in general. In 1940, Churchill<sup>25</sup> reported a series of 124 lobectomies, with a 2.4 per cent mortality. Others reported

no mortality from this operation during recent years Churchill and Belsey<sup>24</sup> gave impetus to the tissue saving operation of segmental resection, particularly as it applied to the lingular segment Graham<sup>26</sup> reported the successful removal of both lower lobes, the right middle lobe, and the lingula of the left upper lobe, in one patient

The treatment of bronchiectasis that is too advanced for surgery is palliative postural and bronchoscopic drainage, penicillin, sulpha drugs, and streptomycin by parenteral or aerosol administration, or sulfa drugs by mouth are all helpful during the acute episodes, vaccines (stock and especially autogenous), general hygienic measures as proper nutrition, including adequate protein and vitamins, attention to the cardiac complications, residence in a warm, dry climate are all useful Climate itself may have an ameliorating influence on bronchiectasis The prompt treatment of acute or chronic sinusitis and tonsilitis cannot be overemphasized, and in spite of the pernicious tendency of many people to overuse vasoconstricting nasal drops until the mucus membranes become swollen and boggy with paralyzed vasoconstricting muscles, the judicious, limited use of vasoconstrictors, in drops or by local application with a cotton tipped applicator, in sinusitis is as well indicated as is incision and drainage for an abscess elsewhere in the body Also, removal of bony or hyperplastic obstructions in the nose are necessary

The proper use of vaccines in early bronchiectasis often gives surprisingly good results at all ages, but especially in children In children the regenerative power is superior, and a defect in a child will be relatively smaller when the part has reached adult growth In using vaccines, it will sometimes be found that the stock vaccine contains antigens closely enough related to the patient's own pathogens that an autogenous vaccine may not be necessary, but more often an autogenous vaccine made from the patient's own sputum becomes preferable

There are several points in the use of vaccines in bronchiectasis that may make the difference between success or failure, in the first place, these treatments must be kept up for long periods of time several years at least, however, after a time, such as a year, the periods between doses, which may have been one week, may be lengthened to two weeks or even a month, and rest periods of a couple of months may be taken The administration should be started with doses small enough to avoid large general and local reactions

While allergy to such extrinsic agents as foods, epidermals, or pollens often precedes infection in the respiratory tract and acts by preparing the tract for chronic sinusitis, bronchitis, or bron-

chiectasis, there are a lesser number of patients in whom the intrinsic infection seems to act as a basic sensitizer, making the patient more susceptible to the extrinsic allergens, and when this happens, the patient may be treated for years with extrinsic allergens without results until the intrinsic bacterial antigen is added. The asthma that develops in middle age after an acute respiratory infection and for which no extrinsic allergenic cause can be found, supports this explanation.

Over twenty years ago, while I was practicing in Colorado Springs, Colorado, the chest specialists there tried out pneumothorax and phrenic paralysis for bronchiectasis, at the same time, these methods were tested extensively elsewhere. Our results were very poor, probably mainly because we chose old, advanced cases with hard, thick, unyielding scar tissue around the dilated bronchi. On the other hand, Hennell<sup>27</sup> reported excellent results recently in four cases of early bronchiectasis by using pneumothorax. This is understandable if the disease is early enough, the collapse squeezes out the infective secretions, it stops the rythmical, respiratory pull on the infection-weakened bronchial walls, it approximates the walls of the infected lung units, and smaller bronchi, which contain little or no cartilage, and thus reduces space for secretions to collect as well as aids fibrotic obliteration, it produces a relative anoxia which inhibits the growth of aerobes, and it produces a slowed circulation with its bacteriostatic and local fibrosing effect. Of course, if the bronchial infection were mainly anaerobic, the collapse therapy in bronchiectasis might encourage the growth of the organisms.

However, minor collapse procedures as Banyai's pneumoperitoneum, phrenic paralysis, and pneumothorax have a very important place as emergency treatments for massive pulmonary hemorrhage in bronchiectasis. Probably the most universally useful one of these is pneumoperitoneum. 1) because it is not always possible to determine immediately which lung is bleeding, 2) the basal portion of the lung, the frequent bleeding site, is often uncollapsible by pneumothorax because of pleural adhesions, 3) pneumoperitoneum is usually the least dangerous and most reversible of these procedures.

### SUMMARY

The incidence of bronchiectasis is greater than generally realized.

Bronchiectasis runs a progressively downward course from its inception, and usually claims its victims in the third decade. Its serious complications are heart failure, metastatic abscesses to the brain and other parts of the body, ankylosis, lung abscess, pleural empyema and attacks of pneumonitis or pneumonia.

Leaving aside congenital bronchial cysts and other developmental malformations, the cause of bronchiectasis is respiratory infection, stenosis of the bronchi, lack of drainage, infection of the bronchial walls with weakening and destruction of the elastic supporting elements, the rythmical inspiratory pull on the weakened walls, which may be augmented by atelectasis or a check-valve mechanism, which increase the stretching effect on the walls

The best treatment for bronchiectasis is prevention or treatment of the early phase removal of a plug of mucus causing atelectasis following bronchial or virus pneumonia or other respiratory infections, prompt treatment of a subacute or chronic bronchitis, prompt treatment of a sinusitis and tonsilitis, attention to respiratory allergies, removal of extrinsic foreign bodies, treatment for endobronchial tumors, extrabronchial tumors and enlarged tracheobronchial and hilar glands, drugs such as sulpha drugs or antibiotics, general hygiene and good nutrition, vaccines (auto-genous or occasionally stock) and sometimes a warm, dry climate

The treatment for advanced bronchiectasis is mainly surgical, if the patient has not advanced to a terminal stage This consists of lobectomy, segmental resection, and occasionally pneumonectomy The younger patient with his superior regenerative power and his greater anatomical and physiological reserves is the preferred surgical risk in operations for bronchiectasis

### RESUMEN

La frecuencia de la bronquiectasia es mayor de lo que generalmente se supone

Desde sus principios la bronquiectasia prosigue un curso progresivamente descendiente y, por lo general, reclama sus víctimas en la tercera década Sus complicaciones graves son insuficiencia cardíaca, abscesos metastásicos al cerebro o a otras partes del cuerpo, amiloidosis, absceso pulmonar, empiema pleural y ataques de neumonitis o neumonia

Pasando por alto los quistes bronquiales congenitos y otras anomalías del desarrollo, la causa de la bronquiectasia es la infección respiratoria, la estenosis de los bronquios, la falta de canalización, la infección de las paredes bronquiales con debilitamiento y destrucción de los elementos elásticos de soporte, la tensión respiratoria rítmica sobre las paredes debilitadas, lo que puede ser aumentado por atelectasia o un mecanismo de válvula de retención que aumenta el efecto de la tensión sobre las paredes

El mejor tratamiento de la bronquiectasia es la profilaxia, o sea el tratamiento de la fase temprana la extracción de un tapón de moco que cause atelectasia subsiguiente a una bronconeumonía o neumonía de virus o a otras infecciones respira-



torias, el tratamiento oportuno de la bronquitis subaguda o crónica, el tratamiento oportuno de senositis y tonsilitis, el tratamiento de las alergias respiratorias, la extracción de cuerpos extraños extrínsecos, el tratamiento de tumores endobronquiales o extrabronquiales y de ganglios tráqueobronquiales e hiliares hipertrofiados, el empleo de drogas, tales como las sulfonamidas o los antibióticos, la higiene general y la buena alimentación, las vacunas (autógenas u, ocasionalmente, no autógenas) y, a veces, un clima cálido y seco

El tratamiento de la bronquiectasia avanzada es principalmente quirurgico, si el paciente no ha avanzado a un estado terminal. Este tratamiento consiste de lobectomía, resección segmentaria y, ocasionalmente neumonectomía. El paciente más joven, con su superior poder regenerativo y sus mayores reservas anatómicas y fisiológicas es el riesgo quirurgico preferido en operaciones para la bronquiectasia.

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# A Case of Aspergillosis of the Lung

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Aspergillosis of the lung is a very rare disease and is due chiefly to the *Aspergillus fumigatus*, but sometimes to *A. niger*, and, even more rarely, to the *Aspergillus flavus*. This disease is usually confused with pulmonary tuberculosis, and, in fact, sometimes co-exists with it. Because there are on record very few such cases not co-existent with pulmonary tuberculosis, we have thought it desirable to describe our case of aspergillosis of the lung, which for a long time was treated as pulmonary tuberculosis.

L. P., 45 years of age, a civil servant. Between 1941 and 1944 he had mild but frequent hemoptyses which subsided without treatment and which were followed by a light paroxysmal cough without expectoration. In 1945 he noticed general weakness of the body, slight loss of weight, a slight evening rise in temperature, an increase in cough with either a great deal of expectoration of pus and mucus or expectoration of blood, as well as such nervous disturbances as insomnia, numbness of the limbs, and undue fatigue. At this time the diagnosis of pulmonary tuberculosis was made and the patient was offered appropriate treatment.

However, in spite of the clinical and x-ray findings, his sputum was consistently negative for acid-fast bacilli on simple smears and concentrates. The patient remained at rest for many months. But in spite of this general treatment, he failed to improve and on April 15, 1946, he came to us for examination.

During the examination of the patient, we were impressed by the characteristic expectoration containing many small, hard, yellowish or whitish grains of varying sizes, and the sputum being consistently negative for tubercle bacilli. Sputum cultures revealed *Aspergillus fumigatus*.

The spores of these fungi are usually found spread on the ground, in the dust of dry leaves and in chaff, and reach the lungs by inhalation. These spores are usually not dangerous. They take on a pathogenic character, however, in cases of lowered resistance, such as, during convalescence after serious communicable diseases, and during chronic illnesses such as diabetes, etc. They are occasionally found as secondary invaders in bronchiectasis, chronic bronchitis, and pulmonary tuberculosis. The disease usually appears in those who are occupied in breeding pigeons (in fact, in bird-breeders in general), and in those whose occupation necessitates their coming into contact with the flour of rye.

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Aspergillosis of the lung can be either primary or secondary. The primary form appears as bronchial or bronchopneumonic. Aspergillar bronchitis is manifested at first by a persistent and paroxysmal cough, and is later followed by a great deal of expectoration, it is also sometimes the cause of bronchial asthma. When the fungus is carried through the bronchi and is located in the lung tissue, the disease then takes the bronchopneumonic form and is followed, in addition to the above symptoms, by frequent hemoptyses. The sputum has a characteristic appearance because in it appear a great many whitish or yellowish granules due to necrosis of the lung tissue. Aspergillosis is usually confused with pulmonary tuberculosis because it is located in the upper lobes.



FIGURE 1 Infiltrating lesions in the right lung and the left lower lobe due to Aspergillosis



FIGURE 2 The same case after four months treatment showing some resolution of the infiltrations

and apices. But the clinical picture of aspergillosis of the lung appears much less serious than some forms of pulmonary tuberculosis because in its first stages it usually develops without fever and does not influence the general condition of the patient. However, in its later stages it brings about considerable lowering of the general condition. Differential diagnosis is possible only through the discovery of the pathogenic factor in the sputum.

Pathologically, aspergillosis of the lung causes necrotic areas of the mucosa and of the lung tissue, of a gray or green-gray color, which are surrounded by other cellular elements that are in different stages of the degeneration. Around these areas, the lung shows chronic infiltration, more or less diffuse. The necrotic areas usually communicate with the lumens of the bronchi, and necrotic tissue is expelled by cough and cavities are formed which differ from gangrene only in the absence of foetid breath. This chronic inflammation of the lungs can spread out and contribute to the hardening of the whole of one or both lungs.

In certain cases, in spite of the presence of small cavities, there are no symptoms. Usually, however, there appear such symptoms (similar to those of pulmonary tuberculosis or chronic bronchitis) as cough with pus and mucus, and, more usually, bloody expectoration with, sometimes, the expulsion of the necrotic lung tissue as well.

The disease can sometimes, but only very rarely, heal spontaneously, leaving behind a general lung cirrhosis.

In our case, we applied the treatment of sulfathiazole, giving by mouth four grams daily in three-hourly doses, and adding some sodium bicarbonate. We continued this treatment for four months, except for some slight interruptions, and gave a total of 420 grams of sulfathiazole which the patient tolerated well. Simultaneously, the patient was taking small quantities of potassium iodide which had to be abandoned after the first month because he was unable to tolerate this. After the second month the expectoration decreased considerably and the sputum changed steadily into mucus, and all the necrotic elements and blood disappeared. Sputum cultures have been negative, and the patient has been in an excellent condition for more than a year. He has returned to work and no longer has any complaints.

### SUMMARY

A case of pulmonary aspergillosis treated as pulmonary tuberculosis for many years has been discussed. The character of the sputum and the persistently negative examination for tubercle bacilli led to repeated cultures of the sputum with the aspergillus

fumigatus finally being recovered Treatment with sulfathiazole and potassium iodide has produced complete cure within 5 months

#### RESUMEN

Se discute un caso de aspergilosis pulmonar que fue tratado como tuberculosis pulmonar por muchos años El caracter del esputo y el hecho de que la busca de bacilos tuberculosos siempre resultó negativa, necesitaron que se hicieran repetidos cultivos del esputo, hasta que al fin se encontro el aspergillus fumigatus El tratamiento con el sulfatiazol y el yoduro de potasio produjo una curación completa en menos de cinco meses

# Atelectasis of the Right Upper Lobe

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JULIO MATA MARTINEZ, M D , F C C P \*\*

Guayaquil, Ecuador

The case that we are going to present, according to its principal complication, atelectasis, contains nothing of particular interest, as these cases become every day more easily recognized and diagnosed. However certain circumstances of its development, the indefiniteness of its etiology, and above all the radiologic changes observed in different phases suggested a diagnosis of carcinoma of the lung, which fortunately was subsequently found to be incorrect.

R L , 52 European refugee, electrician, consulted us for the first time on the 28th of November 1946, with the following complaints—wheezing cough, tenacious muco-purulent expectoration, moderate dyspnea, aggravated by strain and loss of strength, weight and appetite. These symptoms began in May of the same year but in a mild form that did not keep the patient from work. In July he consulted a doctor and at this time his first x-ray film was taken, on the basis of which bed rest was recommended. The patient did not follow the advice, thinking it unnecessary. As his symptoms were not so severe as to hamper his work, he succeeded in staying up and about until in November the cough and dyspnea increased, obliging him to cut down his activities.

At this time we examined the patient noting among other things, exhaustion and debility and his labored respiration even while in a sitting position. Examination of his circulatory system showed little, pulse, 90, regular as to rate, rhythm and intensity, auscultation of heart, negative, blood pressure, 115/70. The respiratory apparatus was carefully examined, with the findings of pharyngitis, imbedded infected tonsils with grade 2 hypertrophy, rhinopharyngitis, and a slight muco-purulent postnasal drip. The right maxillary sinus was somewhat opaque on x-ray examination but puncture revealed nothing. The examination of the lung showed equal amplitude in the respiratory movements, the percussion note was resonant throughout, except in the upper third of the right thorax where impairment was noted. Auscultation showed increased breath sounds and sibilant rales and rhonchi in both lungs and, in the area of dullness in the right lung, subcrepitant rales. The temperature was 37° C , weight 128 lbs , urine, clear, amber, negative for albumen, sugar and bile pigments.

The patient said he had never been seriously ill, and in the nine years since he came to Ecuador has suffered only an occasional cold and coryza. He insisted that he had never had any respiratory disease either here or in Europe and reiterated several times, confirmed by his wife

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FIGURE 1



FIGURE 2



FIGURE 3

*Fig 1 (July 16 1946)* Standard roentgenogram of the thorax. Emphasized upper right interlobar fissure. Opacity above the fissure, which gives the impression of being a parenchymal infiltration. In the central portion of this opacity one may observe an elliptical shadow which suggests cavity. Inference: tuberculous infiltration with cavity.—*Fig 2 (December 19 1946)* Marked opacity which occupies the apex and the interclavicular region on the right, having in its inferior limit the form of a double line which passes from above downward and from without inward. This opacity gives the appearance corresponding to atelectasis of the upper lobe which has drawn the interlobar fissure upward and medialward. In association with this the trachea is drawn slightly to the right. In the remaining part of the right lung field one may observe areas of disseminate infiltration which alternate with radiolucent areas which suggest emphysematous bullae. The left lung field presents no pathological change.—*Fig 3 (December 19 1946)* Bucky film. The limits of the opacity in the superior lobe may be seen more clearly. Numerous small radiolucent areas are seen suggesting emphysema.



who was present, that he cannot recall ever having had an illness which confined him to bed. He had never heard of any asthma or similar disease being present in his family. These assurances seemed important since it is rare to find a primary asthma starting in a patient of over 50, and we concluded that the respiratory syndrome was secondary to some lesion in the right apex, first thinking of course of tuberculosis as a possibility which seemed to be confirmed by the first x-ray film, taken in July. X-ray films No 2 and 3 taken on December 19 somewhat confused the picture and we enlarged the scope of possible etiology to three major diseases: early carcinoma, tuberculosis, atypical pneumonia, the latter having developed in the last few days, secondary to some other unknown disease.

Meanwhile the patient's condition became worse, streaks of fresh blood were found in his sputum and on December 5 he began to run an irregular remittent fever which persisted the 24 days he was hospitalized. During this time the following examinations were made: Hemogram and blood count, showing leukocytosis of 12,000 with normal differential count. Sputum, muco-purulent in appearance, tenacious, slight in quantity but many specimens containing blood, sometimes fresh, sometimes old. Eight specimens were examined on different days, including fresh specimen and homogenized and cultured specimens and only pneumococci, Friedlander's bacillus and streptococci were found. No protozoa, mycelia, cells undergoing mitotic changes, or acid-fast bacilli were detected.

The patient was treated with sulfadiazine and penicillin up to 1,800,000 units during which treatment his temperature dropped and his cough,



FIGURE 4



FIGURE 5

*Fig 4 (December 21, 1946)* Right Bronchogram. One observes a block about 3 cm from the beginning of the right superior lobe bronchus. The middle and inferior lobe bronchi are patent. One sees characteristic shadows of bronchiectasis at the level of the tertiary branch bronchi of the middle lobe. *Fig 5 (December 21, 1946)* Roentgenogram after bronchogram. Iodized oil has not penetrated the superior lobe bronchus. One sees the bronchial pattern alveoli corresponding to the other bronchial branches and in some of these, dilatations may be seen.

expectoration and other pulmonary symptoms diminished. Owing to the position of the shadow high in the lung, bronchoscopy would not have given us much information, and we decided rather to do a bronchogram. The bronchus to the right upper lobe was obstructed and the obstruction ended conically (X-ray film No 4) which misled us seriously, since it is generally accepted that this is the usual picture in bronchogenic carcinoma. Shortly thereafter film No 5 was taken to see if it was possible to do a bronchial aspiration, but the x-ray film showed that the obstruction was complete.

Ten days later another bronchogram (X-ray film No 6) was done and on studying it we found evidence that contradicted this former serious diagnosis, since the blockage of the bronchus had not persisted and the atelectasis had decreased appreciably. The patient's condition improved progressively, the fever ebbed, the cough diminished, the sputum volume decreased, and appetite and strength returned so that he left the clinic the first of January. He was seen every 15 days to affirm that all the symptoms, objective and subjective, had completely disappeared. X-ray film No 7, taken on April 10, showed a normal thorax. Weight was 134 lbs, that is higher than when we first saw him. He had already resumed his work without experiencing any of his former discomforts.

The third bronchogram taken April 23 (X-ray films No 8 and 9) showed bronchial dilatation in the right upper and middle lobes, but the respiratory dynamics were established sufficiently to permit the iodized oil to pass into the three tertiary bronchi of the upper lobe. The guinea

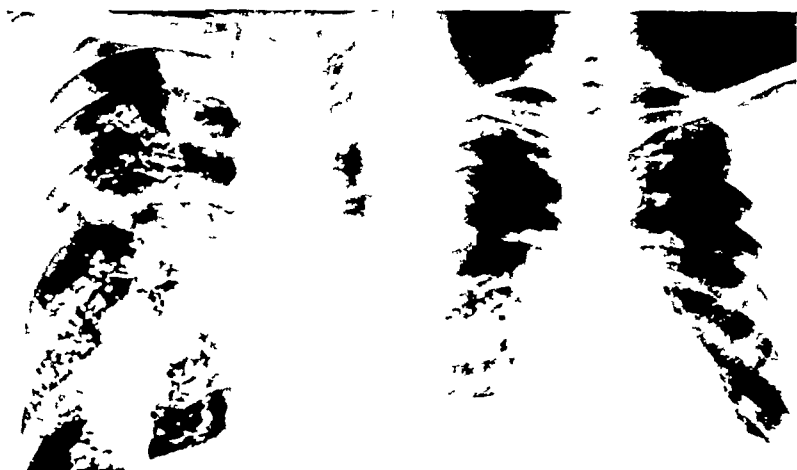


FIGURE 6

FIGURE 7

*Fig 6 (December 31 1946)* Second bronchogram. The bronchial obstruction in the upper lobe has disappeared coincidentally with a manifest diminution in the opacity. Iodized oil has penetrated the axillary and anterior branches of the upper lobe but not the apical branch which corresponds to the area where opacity persists. The position of the right superior lobe bronchus has descended to normal. In these films one sees the right middle and inferior lobe bronchi and their branches. The right main bronchus and the trachea are outlined by the contrast medium. One can see the normal bronchial pattern and several dilated tertiary branch bronchi.—*Fig 7 (April 4 1947)* Both pulmonary fields appear clear. One can see some as yet unexpelled remnants of iodized oil in the right lower lung.

pigs which had been inoculated were killed at the end of the eighth week and showed no pathological change in any of their organs

*Discussion* The symptomatology did not present a true picture in this disease. The physical and laboratory findings were not specifically informative and allowed one only to infer the existence of an inflammatory focus in the right apex, accompanied by bilateral bronchial asthma. The etiological differentiation rested essentially on the x-ray studies done during the course of the disease and confirmed by the clinical findings and additional laboratory information.

Of the radiological evidence, the most important finding was the atelectasis of the right upper lobe, produced by the obstruction of the bronchus to the right upper lobe, as seen in the bronchogram. The atelectasis may have been produced by the following causes:

(1) Intrinsic bronchial obstruction due to—

- a) mechanical action by a foreign body or a mucous plug
- b) endobronchial inflammatory process. For example, tuberculous granulation of the mucous membrane that occludes the bronchus and ulcerations that, invading the bronchial wall, causes scar tissue, which leads to an obstruction.

Furthermore we must not forget that the conditions mentioned act not only by their mere existence but also



FIGURE 8



FIGURE 9

*Fig 8 (April 23, 1947)* Third bronchogram. The three branches of the right upper lobe bronchus are seen by means of filling with the contrast medium.  
*Fig 9 (April 23, 1947)* One can see the three branches of the right upper lobe bronchus and their subdivisions, in which some bronchial dilatation appears. One can also see the branches of the middle and lower lobe bronchi, the former also with some dilatations.

principally in an indirect way, by setting up an inflammation of the mucosa

c) bronchogenic tumor which obstructs as it grows

- (2) External pressure produced by a process generally inflammatory or neoplastic The density of the shadow in the lobe and the conical occlusion that was seen in the first bronchogram indicate why we had at first considered the possibility of a bronchogenic carcinoma of the right lung The continued loss of weight and the blood-streaked sputa seemed to support this, but the rapid restoration of the patency of the bronchus shown in the second bronchogram resolved this doubt

It seems to us that the chronological evolution of this case can be interpreted as follows The patient had, unknown to him, a chronic infection of the upper respiratory system as shown by the post-nasal drip and the opacity of the right maxillary sinus We suppose that at the beginning of his acute illness some mucopurulent plugs from these sites or some locally formed inflammatory products obstructed the bronchus to the right upper lobe There is evidence of this in the first x-ray film, in which the axillary branch of the bronchus seems affected which gave the false impression of a cavity with perifocal reaction This radiographic picture may now be construed as emphysema and partial atelectasis These pathological conditions are enough to explain the asthma-like dyspnea which the patient had suffered for five months before we saw him We suppose in addition that during this long period the bronchial obstruction may have been reversible as well as variable in regards to its position

In the first days of December the development of the obstruction of the trunk of the bronchus to the right upper lobe established the atelectasis of the entire lobe and the consequent infectious process The etiological factors were numerous and some of them were definitely identified pneumococci, Friedlander's bacilli, and streptococci The last bronchogram on April 23 confirmed the complete patency of the bronchus and showed a residual bronchiectasis

### SUMMARY

The authors present a case of pneumopathy of a subchronic type, which became suddenly acute The x-ray films, in which an extensive atelectasis of the right upper lobe was seen, suggested several possible diagnoses, among which were bronchogenic carcinoma and tuberculosis The subsequent development of the acute process eliminated these and pointed clearly to the diagnosis of atelectasis due to bronchial obstruction of an inflammatory origin beginning in a chronic infection of the nasal sinuses

## RESUMEN

Los autores presentan un caso de neumopatía de marcha subcrónica que se agudizó subitamente. Las imágenes radiográficas, en las que se destacaba una atelectasia masiva del lóbulo superior derecho, sugirieron lógicamente varios diagnósticos presuntivos entre los que primaban los de carcinoma broncogenético y tuberculosis. La evolución de la enfermedad eliminó estas hipótesis y permitió definir el diagnóstico de atelectasia por obstrucción bronquial intrínseca de origen inflamatorio determinada por infección crónica de los senos paranasales.

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# The By-Laws

## ARTICLE I

### *Name*

In conformity with its charter this society shall be known as the

AMERICAN COLLEGE OF CHEST  
PHYSICIANS

## ARTICLE II

### *Objectives*

The objectives and purposes of the College shall be

- (a) to establish a world society composed of qualified physicians of high standing who devote all or a major portion of their time to the treatment study or teaching of or to research in diseases of the chest or related specialties,
- (b) to encourage and aid medical colleges in establishing a systematic method of teaching diseases of the chest so as to equip the medical student with a knowledge of the fundamentals which have to do with the technic and importance of early diagnosis the technic and importance of early intensive treatment and the technic and importance of the prevention and control of all diseases of the chest
- (c) to enhance and maintain the interest of practicing physicians in diseases of the chest and to further their training in this specialty
- (d) to maintain and advance the highest possible standards in medical education medical practice and research pertaining to diseases of the chest
- (e) to maintain high standards of specialization among chest physicians and
- (f) to promote the public welfare in connection with the specialty of diseases of the chest

## ARTICLE III

### *Membership*

*Section 1* Members of the College shall be of the following classes Fellows Fellows Emeritus Associate Fellows Associate Members and Honorary Members Fellows shall be entitled to all the privileges of the College including the privilege of voting and holding office Other members shall hold office Only Fellows and Fel-

lows Emeritus shall be privileged to use the letters "FCCP" after their names Other members shall be entitled to all the privileges of the College except the privilege of voting and the privilege of holding office

*Section 2* A roll of all members of the College shall be kept by the Executive Secretary of the College

*Section 3* Qualifications of Fellows and Associate Fellows Every applicant for membership as a Fellow and Associate Fellow shall be prepared to meet the following general requirements

- (a) He shall be the possessor of a diploma conferring the degree of Doctor of Medicine upon him from a medical school acceptable to the Board of Regents
- (b) He shall be a member in good standing of his local state and national medical societies provided however that if he is
  - (1) a full time teacher or research worker in a hospital or institution acceptable to the Board of Regents
  - (2) a medical officer in the service of the United States Government or
  - (3) engaged solely in the public welfare service,the requirement of membership in a local state or national medical society may be waived by the Governor Regent and Chairman of the Board of Regents upon a consideration of his application as provided in Section 7 of this Article III
- (c) He shall be prepared to furnish a written statement setting forth his qualifications and fitness for becoming a Fellow or Associate Fellow of the College as the case may be

In addition every applicant for membership as a Fellow shall be prepared to meet the following requirements

- (a) He shall be more than 29 years of age
- (b) He shall have received his degree of Doctor of Medicine at least 5 years prior to his election to the College
- (c) He shall have had at least 5 years training in the specialty of Diseases of the Chest

(d) He shall be prepared to take a qualification examination to be given from time to time, as the Board of Regents may direct,

and every applicant for membership as an Associate Fellow shall be prepared to meet the following requirements

- (a) He shall be more than 25 years of age,
- (b) He shall have received his degree of Doctor of Medicine at least 2 years prior to his election to the College,
- (c) He shall have had at least 2 years' training in the specialty of Diseases of the Chest

**Section 4 Qualifications of Fellows Emeritus** Every Fellow Emeritus shall have attained the age of 65 years and shall have been a Fellow of the College at least 15 years immediately prior to his designation as a Fellow Emeritus. However, the Board of Regents shall have power to designate such other Fellows as Fellows Emeritus as the Board of Regents may deem proper. Fellows Emeritus shall enjoy all the privileges of the College except the privilege of voting and the privilege of holding office. Should they desire the official publication of the College, they shall pay the regular subscription price.

**Section 5 Qualifications of Associate Members** Every Associate Member shall have met the same requirements as an Associate Fellow except that his work need not consist of such specialties as are required of Associate Fellows but may, at the discretion of the Board of Regents, simply relate thereto.

**Section 6 Qualifications of Honorary Members** The Board of Regents may grant Honorary Membership to such qualified physicians as they may deem to be worthy thereof, in accordance with such rules and regulations as they may from time to time prescribe.

#### **Section 7 Mode of Admission**

(a) An applicant for membership as a Fellow, Associate Fellow, or Associate Member of the College shall

- (1) prepare and submit an application setting forth his qualifications as a Fellow, Associate Fellow or Associate Member, as the case may be, on an application form which may be secured from the

office of the Executive Secretary of the College, and

- (2) deliver the application, together with his dues for the current year and, in the case of a Fellow, his Fellowship fee, and in the case of an Associate Fellow, partial payment of his Fellowship fee, to the Executive Secretary of the College
- (b) If the application is in proper form, the Executive Secretary of the College shall give notice thereof to the Fellows of the College within the metropolitan area in which the applicant resides, or, if the applicant resides in a rural area, to the Fellows of the College within a radius of approximately 100 miles of the place of residence of the applicant, regardless of political boundaries, and shall request them to state the reason or reasons, if any, why the application should not be favorably acted upon
- (c) Two weeks after the mailing of the notice to such Fellows, if the applicant resides in the United States, the Executive Secretary of the College shall forward the application to the Governor for the state wherein the applicant resides, together with a summary of any comments or remarks concerning the applicant submitted by any Fellow of the College
- (d) The Governor shall either approve or disapprove the application. If he disapproves it, he shall send the application to the Regent for the district in which the applicant resides, setting forth the reasons for his disapproval. If he approves it, he shall affix his signature on the application in the space provided thereon, and shall forward it to the Regent for the district in which the applicant resides
- (e) The Regent shall either approve or disapprove the application
  - (1) If he disapproves it, he shall return it to the Governor of the College for the state wherein the applicant resides setting forth the reasons for his disapproval. If he approves it, he shall affix his signature on the application in the space provided thereon and shall forward it

to the Chairman of the Board of Regents

- (2) In the event that the Governor and Regent are unable to agree on the approval or disapproval of the application both the Governor and the Regent shall file a report with the Chairman of the Board of Regents setting forth their reasons for approving or disapproving the application as the case may be
- (f) The Chairman of the Board of Regents shall either approve or disapprove the application and shall present all of the documents to the Board of Regents for final action at their next meeting. The applicant shall be notified of his rejection only after due consideration and final action by the Board of Regents at its next immediate regular meeting
- (g) If the applicant is seeking admission as an Associate Fellow or Associate Member and the Chairman of the Board of Regents approves the application the Chairman shall affix his signature to the application in the space provided for thereon and return it to the Executive Office of the College. The Executive Secretary shall then notify the applicant of his admission
- (h) If the applicant is seeking admission as a Fellow and the Chairman of the Board of Regents approves the application the Chairman shall affix his signature on the application in the space provided for thereon and shall return it to the Executive Office of the College and unless the requirement of examination be waived by the Board of Regents shall direct the Executive Secretary to notify the applicant to appear and take a qualification examination at a time and place specified by the Board of Regents
- (i) (1) If the applicant passes his examination or if the requirement of examination be waived by the Board of Regents the Chairman of the Board of Regents shall so notify the Executive Office of the College in writing and the Executive Secretary shall thereupon inform the applicant that he has been admitted as a Fellow of the College. If the applicant fails to pass his examination the requirement of examination not having been waived by the Board of Regents the Chairman of the Board of Regents shall so notify the applicant and the applicant shall be given the opportunity to take the examination the following year. No candidate shall be permitted to take the examination more than once in a given calendar year and he shall not be given more than three opportunities to pass the examination. In the event that an applicant for Fellowship fails to pass the examination, the Chairman of the Board of Regents shall be authorized to refund without interest 75 per cent of all moneys heretofore paid to the College by the applicant in connection with his application for a Fellowship the remaining 25 per cent being retained to cover the cost incident to examination. If the applicant is rejected for any other reason all moneys without interest, will be refunded
- (2) The rejection of an applicant need not be based upon a mere failure of the applicant to meet the qualifications of Sections 3 or 5 of this Article as the case may be but may rest on any ground which those passing upon such application shall deem sufficient. The Board of Regents may from time to time adopt such additional rules and regulations relating to admissions as it may deem advisable subject to alteration and revision from time to time by the College
- (3) Convocations for confirming certificates of Fellowship of the College shall be held at each annual meeting of the College. All new Fellows shall be required to sign the register of the College at a convocation
- (4) If an applicant seeking admission is affiliated with the medical department of the United States Army United States Navy United States



Air Force, Veterans Administration or Public Health Service, his application shall be submitted to the Governor of the College for that respective service for approval. If the application is approved by the Governor of the College for that service, it shall then be forwarded to the Chairman of the Board of Regents for approval. If the application is approved or disapproved by either the Governor or the Chairman of the Board of Regents, the applicant shall be governed by the rules set forth in Article III, Sections 7 and 8 of the By-Laws.

*Section 8* An Associate Fellow shall make application for membership as a Fellow within five years after his admission as an Associate Fellow of the College. During such period as he remains an Associate Fellow he shall pay yearly installments toward his Fellowship fee as directed by the Board of Regents of the College. In the event that his application for Fellowship is disapproved, any and all moneys paid to the College toward his Fellowship fee shall be refunded to him in full without interest.

*Section 9* Discipline. Any member of the College may be disciplined or expelled for conduct which, in the opinion of the Board of Regents, is unbecoming a Fellow or is derogatory to the dignity of the College or inconsistent with its purposes. The expulsion of a member may only be ordered upon the affirmative vote of two-thirds of the members of the Board of Regents present at a regular or special meeting and only after such member has been informed of the charges against him and has been given an opportunity to present a defense to such charges before the Board of Regents.

#### ARTICLE IV

##### *Officers*

*Section 1* The officers of the College shall consist of a President, a President-Elect, a First Vice-President, a Second Vice-President and a Treasurer.

*Section 2* The President-Elect, the First Vice-President, the Second Vice-President and the Treasurer shall be elected at the annual meeting of the

College, each for a term of one year. The President-Elect shall enter upon his duties as President at the end of the first administrative session of the first annual meeting following his election.

*Section 3* The President of the College shall preside at all regular meetings of the College and at all convocations for conferring certificates of Fellowship of the College. He shall appoint within 60 days after his election to office, members of all councils and standing committees and shall from time to time appoint such other committees as may be necessary or convenient to carry on the activities of the organization. He shall name the chairmen of each council and committee. He shall direct the activities of each council and committee and shall be an ex-officio member of each council and committee except the nominating committee.

*Section 4* The President-Elect shall keep in close touch with the affairs of the College. He shall be an ex-officio member of all committees.

*Section 5* The First Vice-President shall assume the duties of the President in the event of the death, resignation or absence of the President.

*Section 6* The Second Vice-President shall preside at all meetings of the College in the absence of the President and the First Vice-President, and in the event of the death, resignation or disability of the President and the First Vice-President, he shall perform the duties and exercise the power of the President.

*Section 7* The Treasurer shall sign all checks and other documents dealing with the financial transactions of the College. He shall authorize the deposit of all funds of the College in a bank approved by the Board of Regents and dispense same on checks, signed by him and by the auditor of the College, upon receipt of vouchers signed by the Executive Secretary. In his absence, and for limited periods of time, he may delegate the power of receiving and disbursing the funds of the College to an acting Treasurer appointed by the President. At each annual meeting of the College the Treasurer shall submit to the Board of Regents a detailed statement of the financial condition of the College for the fiscal year ending December 31, approved by a certified public accountant, which shall reflect the amount of moneys he has

received and expended during the past year He shall furnish with such statement a written report summarizing the statement He shall further instruct the Executive Secretary to notify the membership at large of the financial condition of the College either by letter or in the official publication of the organization He shall have access to the safety vaults in the presence of the Executive Secretary or his bonded designated assistant for the inspection deposit or withdrawal of securities or other valuable property of the College He shall be bonded in the name of the College for an amount as may be designated by the Board of Regents for the faithful performance of his trust the premium of which shall be paid by the College

## ARTICLE V

### *Board of Regents*

*Section 1* The Board of Regents shall consist of the Past-Presidents of the College the President the President-Elect the First Vice-President the Second Vice-President the Treasurer the Chairman of the Board of Regents and one Regent elected from each regional district of the College The Chairman of the Board of Governors for the College shall be an ex-officio member of the Board of Regents with the right to vote The Executive Secretary or one of his designated assistants shall serve as Secretary to the Board of Regents

*Section 2* One of the members of the Board of Regents shall be elected as its Chairman by a majority vote of the members of the Board of Regents present at an annual meeting and one of the members of the Board of Regents shall be elected as Vice-Chairman by a majority of votes of the members of the Board of Regents present at an annual meeting The Chairman and the Vice-Chairman shall serve for a period of one year and shall be eligible for re-election at each annual meeting Should the Chairman be an elected member of the Board the President shall appoint a Fellow from the regional district of the Chairman as Regent to replace the Regent elected as the Chairman of the Board of Regents

*Section 3* The elected members of the Board shall each serve for a term of three years and no member may serve more than three consecutive terms provided however that at the first election of the Board approximately one-third of the elected

members shall be elected for a one-year term approximately one-third for a two-year term and the remaining one-third for a three-year term The original division of the members into approximate thirds shall be made by the President of the College

*Section 4* In general the Board shall be the business managers of the College Specifically they shall have power to regulate and conserve property interests of the College to fix the annual dues of members to adopt from time to time rules and regulations for the election of Fellows and Associates to the College including the giving of examinations supplementary to and not conflicting with the regulations contained in these By-Laws to determine what publications are to be sponsored by the College to make contracts in connection therewith and to name editorial boards for each publication sponsored to grant charters to state territory and district organizations to divide the states territories and foreign countries having members in the College into appropriate regional districts and to assign the supervision of each such district to a member of the Board and to transact any and all business not otherwise provided for pertaining to the organization and operation of the College

*Section 5* Ten members of the Board shall constitute a quorum for the transaction of business Any Regent may be represented by a Fellow of the College in good standing who holds his written proxy and who resides in the regional district represented by such Regent

*Section 6* There shall be an annual meeting of the Board of Regents at the regular annual meeting of the College and when necessary a semi-annual meeting to be held at a place designated by the Executive Council Additional special meetings of the Board may be called by the Chairman or the President upon a written request therefor signed by eleven members of the Board The Chairman shall preside at all meetings In his absence the President shall preside

*Section 7* During the interim periods between meetings of the Board the business affairs of the College shall be managed by an Executive Council composed of the President the President-Elect the First Vice-President the Second Vice-President the Treasurer and the Chairman and one elected member of the Board of Re-

gents The Executive Secretary shall be the Secretary of the Executive Council The Past-Presidents of the College shall serve as ex-officio members of the Executive Council

*Section 8* Whenever a vacancy may occur among the elected members of the Board, the President shall appoint a Fellow from the regional district represented by the Regent whose place is vacant to fill the vacancy until the next annual meeting of the College, at which time the College shall elect a member to fill the vacancy

*Section 9* The Board may from time to time relocate the states, territories and foreign countries into different regional districts and may increase the number of regional districts

*Section 10* The Board shall appoint an Executive Secretary who shall have supervision of the activities and business affairs of the College The Executive Secretary, or one of his designated assistants, shall (1) act as Secretary to the Board of Regents the Executive Council and the Board of Governors, (2) direct the Executive Offices of the College, maintaining therein all records, such as those of membership inventories and accountings (3) prepare a budget covering all expenditures of the organization for submission to, and approval of, the Board of Regents, (4) direct the mailing of all notices and other forms to be sent to the membership or to the members of the Board of Regents and the Board of Governors, (5) to coordinate the activities of the various College chapters councils and committees and (6) to perform such other duties as may be assigned to him from time to time by the various governing bodies of the College No agreement entered into by the Board of Regents for the services of an Executive Secretary may be of more than three years' duration

## ARTICLE VI

### *Board of Governors*

*Section 1* The Board of Governors of the College shall be composed of members of the College to be elected as provided in Section 3 of this article at each annual meeting of the College as follows One member shall be elected from each state, territory or possession of the United States which has one or more Fellows of the College, one member shall be elected from each of the following services The United States Army, the United

States Navy, the United States Air Force, the Veterans Administration, Public Health Service and the United States Indian Service, and one member shall be elected from each foreign country which has one or more Fellows of the College Whenever a vacancy may occur in the membership of the Board of Governors, the President of the College may appoint a Fellow from the same state, territory, possession, medical service or country formerly represented by the Governor whose place is vacant, to fill the vacancy until the next annual meeting of the College

*Section 2* The Board shall elect one of its members to serve as Chairman of the Board for a period of one year and he shall be a member of the Board of Regents The Chairman may be re-elected for not more than three consecutive terms

*Section 3* The elected members of the Board of Governors shall each serve for a term of three years, provided, however, that at the first election of the Board approximately one-third of the elected members shall be elected for a one-year term, approximately one-third shall be elected for a two-year term, and the remaining one-third shall be elected for a three-year term Thereafter all members shall be elected for a three-year term The original division of the members into approximate thirds shall be made by the President of the College

*Section 4* It shall be the duty of the individual Governors to coordinate and further the best interests of the College in their respective states, territories, possessions, medical services or countries, as the case may be, and to perform such other duties as may be assigned to them by the Board of Regents

*Section 5* The Board shall meet in annual session at the annual meeting of the College or at the call of the Chairman with the approval of the President of the College

*Section 6* In the event that a member of the Board is unable to attend the meeting he may be represented by a Fellow of the College in good standing who holds his written proxy, and who resides within the same state, territory, possession or country represented by the Governor, or who is a member of the same medical service represented by the Governor, as the case may be

*Section 7* No member of the Board of Governors except its Chairman may at the same time be a member of the Board of Regents

*Section 8* The Executive Secretary of the College or one of his designated assistants acting in his behalf shall serve as Secretary of the Board of Governors

## ARTICLE VII

### Fees

*Section 1* A Fellowship fee shall be required of all Fellows of the College subject however to the provisions of Section 2 of this Article VII Annual dues shall be required of all members of the College except Honorary Members and Fellows Emeritus The amount of the Fellowship fee and of the annual dues of members shall be determined by the Board of Regents

*Section 2* At the discretion of the Board of Regents and without publicity any Fellowship fee or annual dues may be waived in whole or in part

*Section 3* Dues shall be payable on January 1 of each year and shall become delinquent if not paid by July 1 of that year A member who is delinquent in his dues automatically loses all privileges of the College including subscription to the official publication A member whose dues are delinquent shall be notified of such delinquency by a regular letter and on September 1 he shall be notified by a registered letter with return receipt requested The notification shall contain formal notice that the member is delinquent in the payment of his dues and that if the dues are not paid by December 31 of that year he will be dropped from the rolls of the College If the dues are not paid by December 31 one year from the time his dues become payable the member shall be dropped from the rolls by order of the Board of Regents

*Section 4* Any member dropped from membership because of delinquency who desires to re-establish his membership must file a new application therefor and must pay the regular Fellowship fee if he was a Fellow and the current dues then required by the Board of Regents together with all past unpaid dues unless waived in whole or in part by the Board

## ARTICLE VIII

### Publications

*Section 1* The Board of Regents through the Executive Secretary shall issue from time to time a directory of the College containing the names and addresses of the members of the College and designating those members who are qualified to administer pneumothorax treatments or who are qualified in any related branch of the specialty of diseases of the chest The Board may also sponsor such other publications as it deems desirable and in the interests of the College

*Section 2* Editorial Boards for publications sponsored by the College shall be composed of Fellows of the College and shall consist of not less than three or more than five members

*Section 3* Each Editorial Board shall have authority to enter into contracts subject to the approval of the Board of Regents or to make other arrangements for the production and distribution of its publications and shall have the power to elect associate editors to its staff from the members of the College

*Section 4* The editorial policy of each publication shall be in accord with the objectives of the College A majority of the members of an Editorial Board shall be required to approve the publication of any material in its publication which any member of such Board considers a matter of policy Each Editorial Board shall be responsible to the Board of Regents of the College

*Section 5* The Editorial Board of the publication which is designated by the Board of Regents as the official organ of the College shall be required to publish in that journal a summary of the transactions of the annual meetings of the College and of the meetings of the Board of Regents

*Section 6* The Board of Regents shall elect the members of the Editorial Board and provide a term of office for each member not to exceed three years and shall also provide that the terms of each member of the board be staggered Any member of an Editorial Board who has served three years may be re-elected for three years upon the recommendation of the other members of the Editorial Board Any new members elected to the Editorial Board should first receive approval of the members of the Editorial Board Each Editorial Board shall elect from among its own mem-

bers a Chairman who shall act as Editor-in-Chief of its publication

## ARTICLE IX

### *Meetings*

*Section 1* An annual meeting of the College shall be held each year, immediately preceding or immediately following the meeting of the American Medical Association, as may be designated by the Board of Regents and in the same city as that meeting, for the election of officers and for the transaction of such other business as may be necessary

(a) The Board of Regents may, if desirable, authorize the Executive Secretary of the College to select a city other than the city in which the American Medical Association meets, for the holding of annual meetings of the College

*Section 2* The College shall conduct scientific sessions at each annual meeting, which shall be devoted to diseases of the chest. The scientific sessions shall be open to all legally licensed physicians, graduate and undergraduate students of medicine

*Section 3* The President shall appoint committees to assist in the arrangements for the annual meetings

## ARTICLE X

### *Councils and Committees*

*Section 1* All councils and committees of the College shall be appointed by the President, who shall designate a chairman, vice-chairman and secretary of each council and committee. Members of councils and committees shall be both individually and collectively responsible to the Board of Regents for the conduct of their respective organizations. Reports and other publications of all councils and committees shall be approved by the Board of Regents before clearance for publication

*Section 2* Each council and committee shall be empowered to further to their best ability the purposes for which it has been established, in accordance with the objects of the College. All councils and committees shall be required to render a report concerning their activities at the annual meeting of the College, or as otherwise directed by the President

*Section 3* The Chairman of each council and committee, unless exempted from this duty by the President, shall be required to furnish to the President an outline of the projects to be carried out by his council

or committee within 90 days after he has accepted the Chairmanship of such council or committee

*Section 4* (a) The following councils, consisting of nine members each, shall be appointed

Council on Undergraduate Medical Education,  
Council on Postgraduate Medical Education,  
Council on Public Health,  
Council of Tuberculosis Hospitals,  
Council of Tuberculosis Committees,  
Council on the Management and Treatment of Diseases of the Chest,  
Council on Public Relations

At the first appointment of these councils three of such members shall be appointed for a one-year term, three for a two-year term, and three for a three-year term. Every year thereafter three members shall be appointed for a three-year term

(b) The number of members of each of the following councils shall be determined by the President. Each member shall serve for a one-year term

Council on International Affairs,  
Council on Pan American Affairs,  
Council on European Affairs,  
Council on Pan Pacific Affairs,  
Council on African and Near East Affairs

(c) The Council on Research shall be composed of two sections, the Financial Section and the Scientific Section

(1) The Financial Section shall consist of nine members, each member to serve for a period of three years and the terms of office shall be staggered so that three new members are appointed each year by the President with the advice and consent of the Board of Regents. The President shall appoint or re-appoint as chairman one of the senior members of the Section. The duties of the Financial Section shall be to raise funds to carry on the work of the council and to secure potentially available endowments and grants

(2) The Scientific Section shall consist of five members whose terms of office shall be staggered so that one member

will serve for five years one for four years one for three years one for two years and one for one year and that one member shall be appointed each year thereafter by the President for a term of five years with the advice and consent of the Board of Regents The President shall appoint a chairman of the Scientific Section with the approval of the Board of Regents The duties of the Scientific Section shall be to consider and approve research projects to be undertaken by the College Their recommendations shall be approved by the Council on Research before being presented to the Board of Regents

- (3) There shall be a general chairman of the Council to coordinate the activities of the Financial Section and the Scientific Section and he shall be appointed by the President with the approval of the Board of Regents
- (d) All policies programs and expenditures recommended by these councils must be approved by the Board of Regents

*Section 5* (a) There shall be a standing Committee on Constitution and By-Laws composed of five members appointed by the President At the first appointment of this committee one member shall be appointed for a five-year term one for a four-year term one for a three-year term one for a two-year term and one for a one-year term and thereafter one member shall be appointed each year for a term of five years Members shall be eligible for re-appointment

- (b) The duties of the Committee on Constitution and By-Laws shall be to consider all proposed changes for amendments to the Constitution and By-Laws and to study and propose amendments from time to time as changing conditions may demand These recommendations shall be referred to the Board of Regents for approval

*Section 6* The number of members of each of the following committees shall be determined by the President

Each member shall serve for a one-year term and may be re-appointed

Committee on Membership  
Committee on College Awards  
Committee on Scientific Program

*Section 7* The chairmen of councils and standing committees shall appoint such sub-committees to serve under the jurisdiction of the council or committee as the case may be as may be deemed advisable or as directed by the Board of Regents of the College These committees may be discharged by the President or the Board of Regents of the College after they have served their purpose All appointments to sub-committees shall be for a period of one year unless the sub-committee be sooner discharged

*Section 8* There shall also be a Nominating Committee consisting of three Fellows of the College One member shall be a member of the Board of Regents and he shall be elected by the members of the Board of Regents at their annual meeting One member shall be a member of the Board of Governors and he shall be elected by the members of the Board of Governors at their annual meeting The third member of the committee shall be a Fellow at large and he shall be appointed by the President and shall serve as chairman The Nominating Committee shall nominate the following officers

- (1) President-Elect
- (2) First Vice-President
- (3) Second Vice-President
- (4) Treasurer
- (5) Historian
- (6) Regents whose terms expired during the current year and
- (7) Governors whose terms expired during the current year

Nominations by the Nominating Committee shall not preclude nominations from the floor at the elections of the various officers

*Section 9* The President shall appoint a Board of Examiners to consist of three or more members Each member shall serve for a one-year term The President shall appoint a chairman vice-chairman and secretary from among the members of this board Members of this board may be re-appointed The Board of Examiners may call upon any Fellow of the College to assist in examinations

## ARTICLE XI

*Chapters*

**Section 1** State and district chapters of the College may be formed and shall apply to the Board of Regents for a charter. Charters shall be issued upon the following conditions

- a) That all the members of the state or district chapter be duly elected members of the College and in good standing,
- (b) That at least one meeting of such state or district chapter be held at the same city, and on or about the same date, as the annual meeting of the state or district medical society in organized medicine covering the same geographical area, or in connection with a recognized medical school or postgraduate assembly,
- (c) That a minimum of fifteen Fellows, Associate Fellows or Associate Members in any one state, group of states, or territory, constituting a recognized medical district, be enrolled as members of the chapter for the purpose of electing officers and conducting the business of the chapter. All officers shall be elected for a period of one year,
- (d) That the name to be used by such state or district chapter shall be approved by the Board of Regents of the College,
- (e) That the By-Laws of each state or district chapter be approved by the Board of Regents of the College,
- (f) That the state or district chapter be self-supporting,
- (g) That the five immediate past-presidents of the chapter be constituted as an Executive Committee. In inaugurating the Executive Committee, the past-president of the chapter shall serve as chairman until the Executive Committee is comprised of five past-presidents. Thereafter each senior past-president shall serve as the chairman of the Executive Committee, in the proper order, for a period of one year, and each additional past-president shall serve on the Executive Committee for a period of five years. The President, Vice-President, and Secretary-Treasurer of the chapter shall be ex-officio members of the Executive Committee. The activities of the chapter shall be directed by the

officers and members of the Executive Committee. It shall be the duty of the Executive Committee to approve the policy of the chapter and to coordinate its activities. The Executive Committee shall guide the officers of the chapter in the proper performance of the duties and responsibilities.

Charters shall be granted by the Board of Regents upon receipt of a written application therefor, which shall satisfy the foregoing conditions, signed by the duly elected officers of the state or district chapter and directed to the Chairman of the Board of Regents of the College.

**Section 2** Action for the withdrawal of the charter of any state or district chapter may be initiated for cause upon written complaint filed by a Fellow of the College with the chairman of the Board of Regents. Before any charter can be withdrawn the officers, if known, of the state or district chapter shall be given written notice of the charges filed against such chapter and shall be given opportunity to appear at a meeting of the Board of Regents, designated in the notice, to be held not sooner than four weeks after the mailing of such notice and shall be permitted to submit testimony and evidence at such meeting as to why such charter should not be withdrawn. If the officers of the chapter are not known to the Board then such notice shall be given to all known Fellows of the College in that state or district.

## ARTICLE XII

*Membership in Countries Other Than the United States of America*

**Section 1** Objective. It shall be the purpose of the College to extend its objectives into all countries of the world.

**Section 2** Qualifications for Membership. Applicants for membership in countries other than the United States of America shall be classified as Fellows and Associate Members. In countries outside of the United States of America the qualifications for Fellowship and Associate Membership shall be such as the Board of Regents shall establish. Both Fellows and Associate Members in countries other than the United States of America shall be entitled to all the privileges of the College, including the privilege of voting and holding office.

### Section 3 Mode of Admission

(a) The applicant for membership as a Fellow or Associate Member of the College shall

(1) prepare and submit an application setting forth his qualifications as a Fellow or Associate Member as the case may be on an application form which may be secured from the office of the Executive Secretary of the College and

(2) deliver the application together with his dues for the current year and in the case of a Fellow his Fellowship fee, to the Secretary-Treasurer of the chapter of the College in the country wherein the applicant resides or if there is no chapter to the Executive Secretary of the College

(a) The Fellowship fee and dues of each chapter shall be approved by the Board of Regents

(b) In countries where monetary restrictions exist the money shall be deposited in a bank approved by the Board of Regents to the credit of the American College of Chest Physicians. This money may be withdrawn only on the order of the Treasurer of the College

(3) It is the intent of the Board of Regents of the College that examining boards be set up as early as possible in each country and whenever feasible. The examining board shall be chosen by the Board of Regents from the members of the chapter in that country

(b) The application shall be approved by the Governor for the country or the district wherein the applicant resides and if there is a Regent for the country or district the application shall also be approved by the Regent and then submitted to the Chairman of the Board of Regents for final approval. If there is neither a Governor nor a Regent in the country or the district wherein the applicant resides the application is to be sent to the Executive Secretary of the College who shall forward the application to

the Chairman of the Board of Regents for approval

(c) In the event that the Governor and Regent are unable to agree on the approval or disapproval of the application both the Governor and the Regent shall file a report with the Chairman of the Board of Regents setting forth their reasons for approving or disapproving the application as the case may be

**Section 4 Discipline** Any member of the College may be disciplined or expelled for conduct which in the opinion of the Board of Regents is unbecoming a Fellow or is derogatory to the dignity of the College or inconsistent with its purposes. The expulsion of a member may only be ordered upon the affirmative vote of two-thirds of the members of the Board of Regents present at a regular or special meeting and only after such member has been informed of the charges against him and has been given an opportunity to present a defense to such charges before the Board of Regents

**Section 5 Governors** Each country where there are one or more members of the College may have a Governor. Governors shall be nominated and elected at the annual meetings of the College and shall serve for a term of one year. The duties of the Governors shall be the same as set forth in Article VI of these By-Laws with the exception of Section 3

**Section 6 Regents** In countries having College chapters the members of the chapter may petition the Board of Regents of the College for the election of a Regent. Should the petition be granted such Regents shall be nominated and elected at the annual meetings of the College and they shall serve for a term of one year. The duties of such Regents shall be the same as set forth in Article V of these By-Laws with the exception of Section 3

**Section 7 Fees** The Fellowship fees and membership dues in countries other than the United States of America shall be determined by the Board of Regents

### Section 8 Charters

(a) Chapters of the College may be formed in any country and officials of such chapters shall apply to the Board of Regents of



the College for charters. Charters to such chapters shall be issued upon the following conditions

- (1) That all members of the chapter be duly elected members of the College in good standing,
- (2) That at least one meeting of the chapter be held each year for the purpose of conducting a scientific session and electing officers, in addition to conducting all necessary business of the chapter. All officers shall be elected for a period of one year,
- (3) That a minimum of 15 Fellows and/or Associate Members for any one country, state, province, or group of countries, states, and/or provinces, be enrolled as members of such national or district chapters,
- (4) That the name to be used by chapters shall be approved by the Board of Regents of the College,
- (5) That the By-Laws of each chapter be approved by the Board of Regents of the College,
- (6) That the chapters be self-supporting,
- (7) That the five immediate past-presidents of the chapter be constituted as an Executive Committee. In inaugurating the Executive Committee, the past-presidents of the chapter shall serve as chairman until the Executive Committee is comprised of five past-presidents. Thereafter each senior past-president shall serve as the chairman of the Executive Committee, in the proper order, for a period of one year, and each additional past-president shall serve on the Executive Committee for a period of five years. The President, Vice-President, and Secretary-Treasurer of the chapter shall be ex-officio members of the Executive Committee. The activities of the chapter shall be directed by the officers and members of the Executive Committee. It shall be the duty of the Executive Committee to approve the policy of the chapter and

to coordinate its activities. The Executive Committee shall guide the officers of the chapter in the proper performance of the duties and responsibilities

Charters may be granted by the Board of Regents upon receipt of a written application therefor, which shall satisfy the foregoing conditions, signed by the duly elected officers of such chapters and directed to the Chairman of the Board of Regents of the College

- (b) The charter of any country or group of countries having a chapter may be suspended or withdrawn for cause upon written complaint filed by a Fellow of the College with the Chairman of the Board of Regents, setting forth the reasons for requesting such withdrawal. Before any charter can be withdrawn the officers, if known, of the chapter shall be given written notice of the charges filed against such chapter and shall be given an opportunity to appear at a meeting of the Board of Regents, designated in the notice, to be held not sooner than four weeks after the mailing of such notice and shall be permitted to submit testimony and evidence at such meeting as to why such charter should not be withdrawn. If the officers of the chapter are not known to the Board then such notice shall be given to all known Fellows of the College in that country or group of countries
- (c) All members and officials of College chapters shall be responsible for the conduct of their activities to the Council on International Affairs of the College and shall make annual reports to the Council concerning the activities of the College in their respective countries

## ARTICLE XIII

### Amendments

Any Fellow of the College in good standing may initiate a proposal for an amendment to these By-Laws. Such proposal shall be presented in writing to the Executive Secretary of the College who shall submit it to the Committee on Constitution and By-Laws for consideration and report to the Board of Regents at their next meeting. The Board of Regents shall then

vote on the advisability of presenting the proposed amendment to the Fellowship as a whole for its consideration. A majority of the members of the Board of Regents present voting favorably for any proposed change in the By-Laws shall make it mandatory upon the Executive Secretary to notify the Fellowship at large either by letter or through the official publication of the College of the text of the proposed amendment. This notification must be presented to the Fellowship at least sixty days before the annual meeting. The Executive Secretary shall then present the proposed amendment to the Fellowship of the College at the annual meeting for their adoption or rejection. A two-third vote of the Fellows present and voting shall be necessary to adopt an amendment.

#### ARTICLE XIV

##### *Original Members and Officers*

The members of this corporation shall

consist of the members of the American College of Chest Physicians an unincorporated association and such other members as may from time to time hereafter be admitted to membership in accordance with the provisions of these By-Laws. The officers, Regents, Governors, committee members and members of the editorial boards of this corporation shall be the officers, Regents, Governors, committee members and members of the editorial boards of the unincorporated association until such time as their term of office or membership would have expired had the unincorporated association continued in existence.

#### ARTICLE XV

The rules contained in Robert's Rules of Order Revised Edition shall govern the American College of Chest Physicians in all cases to which they are applicable and in which they are not inconsistent with the existing by-laws.

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### COMMITTEE ON COLLEGE BY-LAWS

Charles M. Hendricks, M.D., El Paso, Texas, Chairman  
 Carl H. Gellenthien, M.D., Valmora, New Mexico  
 Minas Joannides, M.D., Chicago, Illinois  
 Hollis E. Johnson, M.D., Nashville, Tennessee  
 Walter E. Vest, M.D., Huntington, West Virginia

At the 13th Annual Meeting of the American College of Chest Physicians held at the Ambassador Hotel, Atlantic City, New Jersey, June 5-8, 1947, a resolution was adopted by the Board of Regents requesting the President to appoint a Committee on College By-Laws. The above committee was appointed by Major General S. U. Marietta, President of the College at that time, and the committee was authorized to study the present by-laws and recommend revisions in order to bring the by-laws up to date.

The first meeting of the committee was held at the Hotel Statler, Washington, D. C., on November 21, 1947, at which time the first draft of the by-laws was studied by the committee. The second meeting of the committee was held at the Congress Hotel, Chicago, Illinois, on June 17, 1948, and a second draft of the revised by-laws was studied. The final draft of the revised by-laws was submitted to the Board of Regents of the College at their semi-annual meeting in Miami Beach, Florida, on October 23, 1948. The Board of Regents of the College approved the by-laws with several minor revisions.

In accord with Article 12 of the College By-Laws, the revised by-laws as approved by the Board of Regents of the College have been published herein and they will be submitted for final approval to the Fellowship of the College at the Administrative Session to be held at the Ambassador Hotel, Atlantic City, New Jersey, on June 4, 1949.

# College Chapter News

## FIFTEENTH ANNUAL MEETING AMERICAN COLLEGE OF CHEST PHYSICIANS

The Fifteenth Annual Meeting of the American College of Chest Physicians will be held at the Ambassador Hotel, Atlantic City, New Jersey, June 2 through 5, 1949, just prior to the annual meeting of the American Medical Association, June 6 through 10. Members are urged to make their hotel reservations at once and may use the form appearing on page xi of this issue for that purpose. A limited number of rooms are available at the Ambassador Hotel for members wishing to remain for both meetings.

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### MISSOURI CHAPTER

The Missouri Chapter of the College held a most successful dinner meeting and scientific session at the Chase Hotel, St. Louis, on November 29, just prior to the opening of the Interim Session of the American Medical Association held in St. Louis. Guest speaker at the dinner was George Saslow, M.D., St. Louis, who spoke on "Psychotherapy in the Treatment of Pulmonary Tuberculosis."

Alfred Goldman, M.D., F.C.C.P., St. Louis, Governor of the College for Missouri, presided at the dinner and introduced George D. Kettelkamp, M.D., F.C.C.P., Koch, President of the Chapter. Mr. Murray Kornfeld, Chicago, Executive Secretary of the College, was introduced and presented a brief talk on the activities of the College.

A number of College Fellows who are Delegates in the House of Delegates of the American Medical Association were present in St. Louis and attended the chapter meeting. They were Walter E. Vest, M.D., F.C.C.P., Huntington, West Virginia, Carl H. Gellenthien, M.D., F.C.C.P., Valmora, New Mexico, Robert H. Hayes, M.D., F.C.C.P., Chicago, Illinois, and Bernard Klein, M.D., F.C.C.P., Joliet, Illinois. Also present were Gerald Beatty, M.D., F.C.C.P., Wilmington, Governor of the College for Delaware, Hugh L. Houston, M.D., F.C.C.P., Murray, Kentucky, President-Elect of the Kentucky State Medical Society, W. Edwin Bird, M.D., Wilmington, Editor of the Delaware State Medical Journal, and Walter S. Broker, M.D., F.C.C.P., of East St. Louis, Illinois.

A. J. Steiner, M.D., F.C.C.P., St. Louis, Secretary of the Missouri Chapter, and Alfred Goldman, M.D., St. Louis, were in charge of arrangements for the meeting.

After the dinner meeting the following scientific program was presented:

"Suppurative Diseases of the Lungs,"

Minas Joannides, M.D., F.C.C.P., Chicago, Illinois

"The Effect of Bronchial Infection on Pulmonary Function,"

Edwin R. Levine, M.D., F.C.C.P., Chicago, Illinois

"Pulmonary Mobilization by Decortication,"

Tom H. Burford, M.D., St. Louis, Missouri

## ACTIVITIES OF COLLEGE MEMBERS IN NEW YORK STATE

The New York State Medical Society will meet in annual session at the Hotel Statler, Buffalo, New York, May 2-5. The annual meeting of the New York State Chapter of the College will meet in conjunction with the meeting of the state medical society.

Nelson W. Strohm, M.D., F.C.C.P., Buffalo, Regent of the College, is Vice-Speaker of the House of Delegates of the New York State Medical Society, and Frederic W. Holcomb, M.D., F.C.C.P., Kingston, is a member of the Council and President of the Third District Medical Society of New York State. Foster Murray, M.D., F.C.C.P., Brooklyn, is Chairman of the Section on Chest Diseases in the state medical society, Samuel A. Thompson, M.D., F.C.C.P., New York City, serves as Secretary, and Grant Thorburn, M.D., F.C.C.P., New York City, President of the New York State Chapter of the College, is Delegate from the Section to the House of Delegates of the state medical society.

Articles by College Fellows recently published in the New York State Journal of Medicine are "Bacterial Filtrates and Autogenous Vaccines in the Treatment of Chronic Sinus Disease and Other Chronic Respiratory Affections," by Hugh M. Kinghorn, M.D., F.C.C.P. and George E. Wilson, M.D., F.C.C.P., Saranac Lake, and "Physical and Roentgenologic Findings in the Early Diagnosis of Nonopaque Foreign Bodies of the Bronchial Tract" by Arthur Q. Penta, M.D., F.C.C.P., Schenectady.

At a meeting of the Saranac Lake Medical Society on November 24, George W. Wright, M.D., F.C.C.P. and R. S. Mitchell, M.D., discussed "Pneumoperitoneum."

The next postgraduate course on diseases of the chest to be given in New York City under the sponsorship of the Council on Postgraduate Medical Education of the College will be held at the Hotel New Yorker, November 14-19, 1949.

For further information concerning the annual meeting of the New York State Chapter of the College please communicate with Donald R. McKay, M.D., F.C.C.P., Secretary of the Chapter, 333 Linwood Avenue, Buffalo, New York.

The present officers of the New York State Chapter are Grant Thorburn, M.D., New York City, President, Roger A. Hemphill, M.D., Mount Morris, First Vice-President, Joseph J. Witt, M.D., Utica, Second Vice-President, and Donald R. McKay, M.D., Buffalo, Secretary-Treasurer. George Foster Herben, M.D., F.C.C.P., Yonkers, is Governor of the College for New York State.

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## ORGANIZATION OF THE NORTHEAST BRAZILIAN CHAPTER

On November 19, 1948, in Recife, Brazil, the 37th Chapter of the American College of Chest Physicians was chartered as the Northeast Brazilian Chapter. Officials of the College who were present at the organization meeting were Lopo de Carvalho, M.D., F.C.C.P., Governor of the College for Portugal, Eduardo T. Etzel, M.D., F.C.C.P., Governor for the Southern Brazilian Chapter, Reginaldo Fernandes, M.D., F.C.C.P., Governor for the Central Brazilian Chapter, Jose Silveira, M.D., F.C.C.P., Governor for the East Brazilian Chapter and Affonso MacDowell Filho, M.D., F.C.C.P., Secretary of the Central Brazilian Chapter.

The following officers were elected for the newly organized Northeast Brazilian Chapter

Joaquim Cavalcanti, M D , Governor  
Agenor de Sousa Bomfim, M D , President  
Joao Asfora, M D , Vice President, State of Pernambuco  
Lourival Moura Dantas, M D , Vice President, State of Paraiba  
Milton Ribeiro Dantas, M D , Vice President, State of Rio Grande do Norte  
Otavio Lobo, M D , Vice President, State of Ceara  
Herodoto Pinheiro Ramos, M D , Secretary  
Manuel Gomes, M D , Treasurer

Among the guests who presented papers at this meeting, which was held in conjunction with the IV National Congress of Tuberculosis, were Felice Parodi, M D , of Italy, Roger Even, M D , of France and Lopo de Carvalho, M D , F C C P , of Portugal

*Northeast Brazilian Chapter Organizational Meeting  
November 19, 1948, Recife, Brazil*



Left to right Reginaldo Fernandez, M D , F C C P , Governor of the Central Brazilian Chapter, Lopo de Carvalho, M D , F C C P , Governor for Portugal, Pinheiro Guimaraes, M D , Affonso MacDowell Filho, M D , F C C P , Secretary of the Central Brazilian Chapter and Roger Even, M D , Guest Speaker, Paris, France

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CENTRAL AMERICAN CHAPTER

The Central American Chapter held its II Annual Reunion at the Sanatorio Antituberculoso, on January 19, 1949, in conjunction with the III Central American Congress of Tuberculosis Enrique Coronado Iturbide, M D , F C C P , Governor of the College for Central America,

is also the President of the III Central American Congress of Tuberculosis Rafael Leal h, M.D, and J Mauricio Gutierrez de Leon, M.D, President and Secretary-Treasurer of the Central American Chapter of the American College of Chest Physicians, respectively, comprise the Board of Directors of the III Central American Congress of Tuberculosis

### PERUVIAN CHAPTER

The Peruvian Chapter of the American College of Chest Physicians held its IV Annual Reunion at the Central Antituberculosis Dispensary in Lima, Peru, during the 20-23 of December, 1948 The following scientific program was presented

*December 20, 1948, 7 P M*

"El Instituto de la Tuberculosis,"

Ovidio Garcia Rosell, M.D, F C C P

"Investigacion Tuberculino-Radiologica en los postulantes a la Universidad Mayor de San Marcos 1947-1948,"

Juan A Werner, M.D, F C C P

"Tuberculosis y Ocupacion,"

Luis E Hubner, M.D, F C C P

"Indice de infeccion y morbilidad tuberculosa en Magdalena Nueva,"

Manuel Agurto, M.D y Tomas Cortez, M.D

*December 21, 1948, 7 P M*

"Cierre Cavitaro por perforacion en el curso del nuemotorax terapeutico,"

Luis Cano Girona, M.D, F C C P

"La Estreptomicina en el tratamiento de la laringitis tuberculosa,"

Leopoldo Molinari, M.D, F C C P

"Formas gangliopulmonares y estreptomicina,"

Mario Pastor, M.D, F C C P

"Tuberculosis gangliopulmonar,"

Victor Narvaez, M.D

"El lavado bronquial en las bronquiectasis," ,

Federico Vargas Jimenez, M.D

*December 22, 1948, 7 P M*

"O M 32 en Tuberculosis,"

Juan A Werner, M.D, F C C P

"Lesiones pulmonares no visibles a la radiografia simple,"

Juan Escudero Villar, M.D, F C C P

"Resultado de las pruebas funcionales y electrocardiograficas en un grupo de operados de toracoplastia,"

Victor Tejada, M.D, F C C P

"Sarcoma del pulmon,"

Carlos Alberto Lopez, M.D, F C C P

*December 23, 1948, 7 P M*

"Tumores broncopulmonares primitivos,"

Max Espinoza Galarza, M.D, F C C P

"Sindrome toraxico-abdominal producido por alteraciones diafragmaticas,"

Ramon Vargas Machuca, M.D, F C C P

"La dihidroestreptomina,"

Leopoldo Molinari, M.D, F C C P

MEETING, ILLINOIS CHAPTER AMERICAN COLLEGE OF CHEST PHYSICIANS  
Congress Hotel, Chicago January 7, 1949



Some of the physicians who were present at the dinner given in honor of Dr Gumersindo Sayago Cordoba Argentina

After the scientific meeting, the following officers were elected for the coming year

Ramon Vargas Machuca, M D , Lima, Peru, President  
Juan Escudero Villar, M D , Lima, Peru, Vice President  
Leopoldo Molinari, M D , Lima, Peru, Secretary  
Luis E Hubner, M D , Callao, Peru, Treasurer  
Luis A Morales, M D , Lima, Peru, Librarian

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#### ILLINOIS CHAPTER

A joint meeting of the Chicago Tuberculosis Society and the Illinois Chapter of the College was held in Chicago at the Congress Hotel on Friday evening, January 7th. A dinner honoring Professor Gumersindo Sayago, F C C P, Cordoba, Argentina, was given just prior to the scientific session. Dr Sayago was guest speaker at the dinner.

The following scientific program was presented after the dinner meeting

"Clinical Application of Dihydrostreptomycin,"  
David T Carr, M D , Department of Medicine, Mayo Clinic  
"Paraminosalicylic Acid in Experimental and Clinical Tuberculosis,"  
Robert H Ebert, M D , University of Chicago  
"Use of Paraminosalicylic Acid in the Treatment of Tuberculosis,"  
Henry C Sweany, M D , F C C P , Medical Director of Research,  
Municipal Tuberculosis Sanitarium  
General Discussion

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#### DOCTOR GUMERSINDO SAYAGO VISITS THE UNITED STATES OF AMERICA

Dr Gumersindo Sayago of Cordoba, Argentina, Regent of the American College of Chest Physicians, and Past President of the Argentine Chapter of the College has visited in the United States after completing a tour of the Philippine Islands for the Mission of the Unitarian Service Committee and the World Health Organization of the United Nations. Dr Sayago was the expert on tuberculosis in a four man commission which was concerned with general health problems in the Philippines. Following completion of the work of the mission, Dr Sayago remained in the Philippines as an official guest of the Philippine Government to institute an intensive training course on BCG vaccination, bacteriological diagnosis and tuberculin testing for physicians and nurses. While in the Philippine Islands, Dr Sayago was honored by being awarded the Medal of Rizal as an Honorary Knight of the Rizal Legion. Dr Sayago also organized the Philippine Chapter of the American College of Chest Physicians and installed the officers of the newly established chapter during his visit.

On December 30 Dr Sayago arrived in San Francisco where he was met by Dr Harry C Warren, Second Vice-President of the College, Dr Seymour M Farber, Secretary-Treasurer of the California Chapter of the College, Dr Sidney Shipman, a Fellow of the College, and Dr George Becker of the San Francisco Public Health Department. Dr Sayago left San Francisco for Minneapolis, arriving there on



January 4, where he was the guest of Dr Jay Arthur Myers, Editor of the College journal, "Diseases of the Chest" While in Minneapolis, he delivered a lecture before a joint meeting of the Minnesota Chapter of the College and the Minnesota Trudeau Society Dr Sumner Cohen, President of the Minnesota Chapter, presided at the meeting

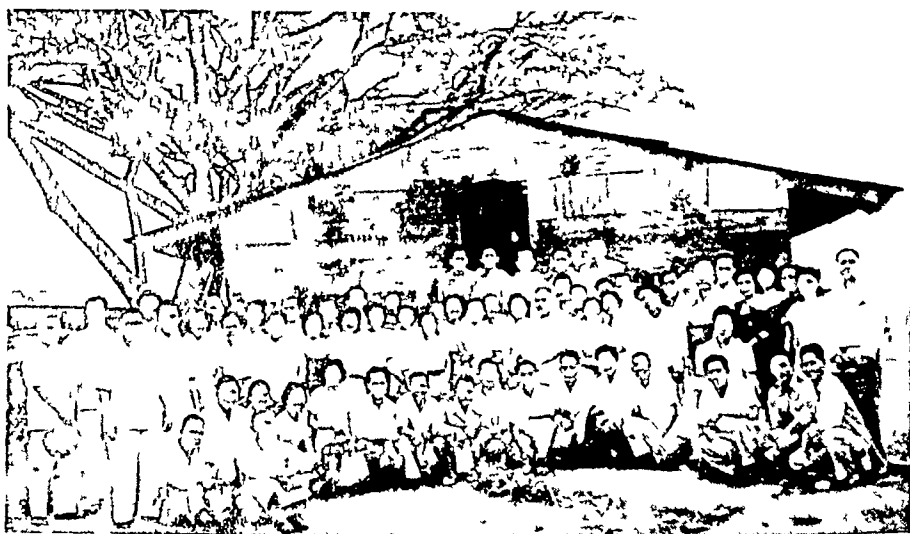
On January 7 Dr Sayago delivered a lecture in Chicago on his mission to the Philippine Islands at a joint meeting of the Illinois Chapter of the College and the Chicago Tuberculosis Society He was introduced at the dinner meeting by Dr Henry C Sweany, a member of the Editorial Board of the College journal During Dr Sayago's stay in Chicago, he spoke at a staff meeting at the Municipal Tuberculosis Sanitarium and also visited the Tice Clinic for BCG of which Dr Sol Roy Rosenthal is director

After leaving Chicago Dr Sayago visited the University of Michigan at Ann Arbor and then proceeded to Boston where he was the guest of Dr Richard H Overholt, President of the College, and Dr Marcio M Bueno, Medical Director of the Tuberculosis Division, Fall River General Hospital

Dr Sayago's next visit was to New York City where a number of meetings were arranged While in New York City he was the guest of Dr Juan R Heriadora, Secretary of the Council on Pan American Affairs of the College On January 20 Dr Sayago delivered a lecture at the Henry Phipps Institute, Philadelphia During his visit there Dr Sayago was the guest of Dr Esmond R Long, Editor of the American Review of Tuberculosis

On January 20 Dr Sayago left New York City for Mexico City to attend the VIII Congress of Latin American Tuberculosis Societies (ULAST) Dr Sayago is a former President of this Society, having presided at the V Congress which was held in Argentina in 1940

During Dr Sayago's visit to the United States, he was entertained by many of his friends



*Staff of Tuberculosis Hospital, Nichols Field, Philippine Islands, taken during the visit of Dr Gumersindo Sayago*

## College News Notes

Richard H Overholt, MD, FCCP, Brookline, Massachusetts, President of the American College of Chest Physicians, will give a lecture on "Surgery's Place in the Treatment of Pulmonary Tuberculosis" on January 18, at Houston, Texas. The lecture will be given at a meeting honoring Dr Elva A Wright John Roberts Phillips, MD, FCCP, Houston, will introduce Dr Overholt. On the following evening Dr Overholt will speak at a meeting of the Harris County Medical Society and his subject will be "Cancer of the Lung"

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Edgar Mayer, MD, FCCP, New York, N Y, Chairman of the Council on African and Near East Affairs of the College, is making a trip to the near east for the World Health Organization. He will visit Turkey, Palestine, Egypt, Lebanon, Iraq, Iran and Syria.

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A Barkhe Coulter, MD, FCCP, Washington, D C, was elected President of the Metropolitan Washington Tuberculosis Conference at a general meeting on October 29 at Glenn Dale Sanatorium. Dr Coulter, who is Director of the District Bureau for Tuberculosis, succeeds Dr V L Ellicott, Health Officer for Montgomery County, Maryland.

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David D Feld, MD, FCCP, former acting medical director of the Los Angeles Sanitarium, has accepted appointment as Medical Director of the Jewish Consumptives Relief Society Sanatorium at Denver, Colo.

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On October 15, ground was broken at Mt Vernon, Illinois for the beginning of construction of the first State-owned tuberculosis hospital for the public in Illinois. The hospital will be known as the Mt Vernon State Tuberculosis Hospital and will be operated under the direct supervision of the State Department of Public Health.

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Edwin R Levine, MD, FCCP, Chicago, Illinois, has been appointed representative of the Scientific Exhibit for the Section on Diseases of the Chest of the American Medical Association to assist in the procurement of exhibits for the 98th Annual Session of the American Medical Association to be held in Atlantic City, June 6-10, 1949.

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Maurice G Buckles, MD, FCCP, Columbus, Ohio, presented an interesting paper on "Recent Developments in Chest Surgery" at the regular monthly meeting of the Cabell County Medical Society, held October 14 at the Hotel Prichard in Huntington.

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The article by Robert B Homan Jr, MD, FCCP, El Paso, Texas, entitled "Tuberculosis and the General Practitioner" has been published in a recent issue of the Texas State Journal of Medicine.

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Henry C Sweany, MD, FCCP, Medical Director of Research at the City of Chicago Municipal Tuberculosis Sanitarium and a member of the Board of Directors of the Tuberculosis Institute of Chicago and Cook County, was awarded the Dearholt Medal by the Mississippi Valley Conference on Tuberculosis. He was cited for his research on bacteriology and pathology of tuberculosis and associated conditions.

Arthur W Newitt, M D , F C C P , formerly head of the Chicago Municipal Tuberculosis Sanitarium, has accepted an appointment as tuberculosis control officer for the state of Michigan

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The first annual Clyde M Fish Memorial Lecture of the Atlantic County Hospital for Tuberculous Diseases, Clyde M Fish Memorial, was delivered on November 18, 1948 by Burgess Gordon, M D , F C C P , Philadelphia, Professor of Medicine, Jefferson Medical College, and Director of the Barton Memorial Division for Chest Diseases, Jefferson Medical College

The address, entitled "Tuberculosis," was open to the profession and to the public The meeting was held at the Haddon Hall Hotel, Atlantic City, and was presided by Charles Hyman, M D , F C C P , Medical Director, Clyde M Fish Memorial

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The Board of Regents has appointed Professor Maurizio Ascoli, M D , F C C P , of Palermo as Governor of the College for Italy

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#### COMMITTEE ON CHEMOTHERAPY AND ANTIBIOTICS

The Committee on Chemotherapy and Antibiotics, which serves under the Council on the Management and Treatment of Diseases of the Chest of the College, recently released a report on "The Use of Streptomycin in Tuberculosis" This report was intended primarily for general practitioners, to keep them informed on the recent developments in the use of streptomycin in tuberculosis Copies of the report were mailed to state, specialty and other medical journals in the United States for publication The report has appeared in the following medical journals

The Journal of the Medical Association of the State of Alabama, December, 1948

The Journal of the Arkansas Medical Society, November, 1948

The Connecticut State Medical Journal, November, 1948

The Journal of the Maine Medical Association, November, 1948

Medical Annals of the District of Columbia, November, 1948

The Military Surgeon, December, 1948

The North Carolina Medical Journal, October, 1948

The Journal of the Ohio State Medical Society, January, 1949

The Texas State Journal of Medicine, December, 1948

The West Virginia Medical Journal, November, 1948

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#### PARA AMINOSALICYLIC ACID

The Panray Corporation is now marketing PAS (Para Aminosalicyclic Acid) to sanatoria, hospitals, and medical research workers

Though still under investigation, PAS is reported to be a promising chemotherapeutic agent in the treatment of tuberculosis Steady supplies are now available for immediate delivery

The company has assembled a complete bibliography of important papers dealing with PAS These are available on request to interested workers Write The Panray Corp , 398 Broadway, New York, N Y

# DISEASES of the CHEST

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## A Comparative Study of Sulfadiazine, Penicillin, and Penicillin Combined with Sulfadiazine in the Treatment of Lobar Pneumonia\*

ITALO F VOLINI, M.D., F C C P JAMES R HUGHES, M D  
and J R PEFFER, M D\*\*  
Chicago Illinois

The efficiency of the therapeutic agents in the treatment of pneumococcic pneumonias has been definitely established at this time. However, the common current use of combinations of these drugs with the hope of enhancing their activity prevails. Recently reported mortalities include those of Anderson and Ferguson 12.7 per cent with sulfathiazole, and 11.1 per cent with parenteral penicillin,<sup>1</sup> Collins, Sellers and Kast 6.7 per cent with combined penicillin and sulfadiazine<sup>2</sup> and our experience in previous surveys of 9.6 per cent with sulfadiazine, 4 per cent with sulfapyridine and 6.3 per cent with oral penicillin.<sup>3,5</sup> The variation in these results is certainly small enough, considering statistical errors, to sanction the use of any method indicated. The ease of administration, cost of medication and complicating toxicities must be considered in choosing the most satisfactory mode of arresting pneumococcic infections. The hazard of sensitivity to sulfonamides, the inconvenience of parenteral administration of penicillin and the possibilities of antagonistic activity in combining both medicaments justifies more specific information in selecting the choice of therapy.

Following a recent analysis of a group of patients treated with oral penicillin for pneumococcic pneumonia at Cook County Hospital, Chicago, Illinois,<sup>5,6</sup> a comparative study was undertaken to

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\*Aided by a grant from the Commercial Solvents Corporation, Terre Haute, Indiana. Presented at the 14th Annual Meeting, American College of Chest Physicians, Chicago, June 20, 1948.

\*\*From the Hektoen Institute for Medical Research of the Cook County Hospital and the Department of Medicine of the Cook County Hospital and Loyola University School of Medicine.

establish the efficiency of oral and parenteral penicillin as contrasted to sulfadiazine and sulfadiazine combined with intramuscular penicillin. Two hundred and thirty nine patients were included in this study. This total number was subdivided relative to type of therapy as indicated in Table I. Group I included ninety cases treated with sulfadiazine, Group II, 54 cases treated with intramuscular crystalline penicillin, Group III, forty eight cases with oral penicillin and Group IV, 47 cases treated with combined penicillin and sulfadiazine.

### *Method*

Since the various medical wards at Cook County Hospital receive new admissions in regular rotation regardless of the type of case or severity of illness, it was possible to obtain a satisfactory therapeutic grouping of patients by dividing the wards into segments and arranging for a uniform type of treatment in each segment. In most cases blood culture and sputum examination were obtained. The sputum type was determined by the Neufeld reaction and when this failed, the sputum was cultured on blood agar plates and retyped if pneumococci were found. Blood cultures were incubated 48 to 72 hours and subcultured. In twenty nine cases where the sputums were negative, pneumococci were obtained in this way. Blood was drawn for a sulfadiazine or a penicillin level 48 hours after the initial medication was administered. Chest x-rays were obtained when necessary to confirm the diagnosis.

### *Dosage and Method of Administration*

Four grams of sulfadiazine were administered as an original dose followed by one gram every four hours around the clock. This was accompanied in most instances by an equal quantity of sodium bicarbonate. Fluids were administered in an amount to insure a daily urinary output of 1500 cc or more. Daily urinalyses and additional blood counts were obtained during the period of drug therapy. This procedure was continued until all of the patients included in this group were afebrile for 48 to 72 hours.

TABLE I

	Type of Therapy	Number of Cases
Group I	Sulfadiazine	90
Group II	I M Penicillin	54
Group III	Oral Penicillin	48
Group IV	I M Penicillin with Sulfadiazine	239
TOTAL		239

Intramuscular penicillin was given in the crystalline form in 20,000 unit quantity. The first dose was 40,000 units. This schedule was maintained in all unless evidences of poor response became apparent whereupon the three hour dose was increased to 30,000 units. Supportive measures were used as indicated. All medications were given until the patients were afebrile for 48 to 72 hours.

The oral penicillin used was pure crystalline potassium penicillin assaying slightly over 1500 units per milligram and containing

TABLE II  
Typed Pneumococccic Pneumonias

Types	Sulfadiazine			I M Penicillin			Oral Penicillin		
	Cases	Bact	Died	Cases	Bact	Died	Cases	Bact	Died
1	7	1	1	5	1		4	3	
2	11	5	3	6	3		9	4	1
3	2			2			1		
4	3			1	1		2	1	
5	4	2	1	2	1		1		
6	2			2			2		
7	4	2	2	2			1		
8				2	1		1	1	
10	3			1			2		
11	1								
12	3			2					
15	1								
16							2		
17	1	1							
33	1								
Pneumococcus failed to type	2	1					1	1	1
TOTAL	45	12	7	25	7		26	10	2
Hemolytic Streptococcus	1		1						
Staphylococcus Aureus	1								
Hemolytic Staphylococcus				1					
Friedlander's Bacillus							1		
Unidentified Bacterial Etiology	43			28		1	21		1
TOTALS	90		8	54		1	48		3

over ninety five per cent penicillin G. Each tablet contained 100,000 units. One hundred thousand units was administered every three hours continuously at 3, 6, 9, and 12 o'clock during the twenty four hours, awakening the patient through the night hours as indicated. A primary dose of 200,000 units was given shortly upon admission to the hospital following the diagnosis of pneumonia. No particular effort was made to separate medication from the ingestion of food as the schedule outlined at the Cook County Hospital permitted both to be given at the same time only at the noon day meal. This method of dosage and drug administration has been reported by us as producing plasma penicillin levels of 0.06 units per cc. or higher during most of the three hour interval between doses. As has been previously indicated,<sup>6</sup> this concentration was found in vitro studies to sterilize cultures of the great majority of strains of the pneumococcus, Group A hemolytic streptococcus, gonococcus and most of the strains of streptococcus viridans.

Combined intramuscular and sulfadiazine was given in the same dosage as indicated in the above individual groups. Here too, supportive treatment was given when indicated.

### Results

Patients in the four therapeutic groups were admitted to the medical wards in the same pneumonia season 1945-1946. Although variations in the symptomatic and supportive measures were adapted to the individual patient, no attempt was made to reserve any of the specific therapy for certain chosen patients. The severity of the pneumonias used in this study is indicated by the incidence of the most virulent pneumococcal organisms, the frequency of multilobar involvement, the presence of bacteremia, associated diseases, the duration of the disease prior to therapy and the age of the patients so infected.

TABLE III  
Comparison of Groups and Severity of Illness

	GROUP I <i>Per cent</i>	GROUP II <i>Per cent</i>	GROUP III <i>Per cent</i>	GROUP IV <i>Per cent</i>
Incidence of types 1, 2, 3, 7 and 8	53.3	68	61.5	
Bacteremia	26.7	28	38.5	
Duration of disease prior to treatment	4.27	3.89	3.78	3.56
Multilobar involvement	20.0	23.5	29.2	27.3
Age over 50	35.6	22.2	35.4	31.9

Forty five of the 90 cases in the sulfadiazine treated patients (Group I) proved to be of pneumococcic origin (Table II) while 24 (53.3 per cent) of these (Table III) were classified to be of Types I, II, III, VII, or VIII. Group II included 68 per cent of these more serious invaders while Group III showed an incidence of 61.5 per cent. The Bacteremic incidence is indicated as 26.7 per cent, 28 per cent, and 38.5 per cent in the first three respective groups suggesting a more seriously ill class of patients who received oral penicillin. Multilobar involvement was highest in this group also (Table III) being 29.2 per cent as compared to 20.0 per cent, 23.5 per cent, and 27.3 per cent in Groups I, II, and IV, respectively. The duration of treatment prior to therapy was quite constant throughout being somewhat delayed, however, in the sulfadiazine group. These patients also showed the highest incidence of age over 50 (35.6 per cent), the lowest being 22.2 per cent, in those cases receiving intramuscular penicillin. Sputum culture, typing and blood culture studies were not available in the pneumonias classified in Group IV. However, the duration of the disease prior to treatment, incidence of multilobar involvement and percentage of cases over 50 years of age suggest that these patients were somewhat less severely ill than those treated with sulfadiazine alone or those receiving oral penicillin in Group III. Further evidence indicating this is apparent from the very low number of cases, 15 per cent (Table V) in Group IV having associated

TABLE IV  
Mortality According to Age Groups

Age	GROUP I Sulfadiazine			GROUP II I M Penicillin		
	Cases	Died	Per cent	Cases	Died	Per cent
Under 50 years	55	7	12.7	41	1	2.4
Over 50 years	32	1	3.1	12	0	0.0
Age unknown	3	0	0.0	1	0	0.0
TOTALS	90	8	8.9	54	1	1.9

TABLE IV (Continued)

Age	GROUP III Oral Penicillin			GROUP IV Penicillin and Sulfadiazine		
	Cases	Died	Per cent	Cases	Died	Per cent
Under 50 years	31	1	3.2	32	3	9.4
Over 50 years	17	2	11.8	15	2	13.3
Age unknown	0	0	0.0	0	0	0.0
TOTALS	48	3	6.25	47	5	10.6



disease It seems most probable, therefore, that the highest incidence of severe illness was in Group III, those patients receiving oral penicillin The remaining groups showed approximately equal complicating factors

All of these cases included in this study are probably not repre-

TABLE V  
Associated Diseases

Group I — Sulfadiazine 26 cases or 29 per cent	
Chronic alcoholism	11
Cirrhosis of liver	1
Latent lues	3
Bronchial asthma	1
Low grade prostatitis and cystitis	1
Severe pyelonephritis	1
Rheumatic heart disease, compensated	1
Hypertensive heart disease, compensated	1
Diabetes mellitus, mild	1
Avitaminosis	2
Arteriosclerotic heart disease	1
Pulmonary tuberculosis	1
Cellulitis and lymphangitis thigh from burn	1
Group II — I M Penicillin 13 cases or 24 per cent	
Chronic alcoholism	8
Cirrhosis of liver	1
Latent lues	1
Epilepsy	1
Rheumatic heart disease, compensated	1
Congenital deformity of thorax with scoliosis	1
Group III — Oral Penicillin 17 cases or 35 per cent	
Chronic alcoholism	6
Cirrhosis	2
Pulmonary tuberculosis	3
Hypertensive heart disease	1
Bronchial asthma	1
Bronchiectasis with pulmonary arthropathy and arteriosclerosis	1
Arteriosclerotic heart disease with auricular fibrillation, decompensated	1
Rheumatic heart disease, compensated	1
Acute pyelitis	1
Group IV — Penicillin combined with Sulfadiazine 7 cases or 15 per cent	
Chronic alcoholism	3
Arteriosclerotic heart disease, compensated	2
Arteriosclerotic hypertensive heart disease, compensated	1
CNS lues	1

sentative of the average pneumonia encountered in routine practice because of the frequency of prolonged exposure noted prior to hospitalization and a greater incidence of malnutrition encountered in patients entering a large charitable institution. The pneumonias under consideration here, therefore, are considered to be representative of the more severe cases of pneumonic infection than those seen in every day medical practice.

Blood concentrations of the therapeutic agents used were determined in all patients and these have been reported as adequate for the *in vitro* sensitivities of pneumococci recovered on culture. It is not the purpose of this paper to indicate clinical febrile response or efficiency of individual type of therapy as this has been reported by us in numerous previous publications. These results are considered on a comparative basis only, the relative efficiency of treatments.

Adequate therapeutic response was measured by the effect of therapy on fever, the mortality rate, the duration of treatment and the incidence of complications in the various therapeutic groups. A comparison of clinical febrile control is indicated in

TABLE VI  
Duration of Treatment

Days	GROUP I Sulfadiazine	GROUP II I M Penicillin	GROUP III Oral Penicillin	GROUP IV Penicillin with Sulfadiazine
Average duration treatment	6.9	5.5	5.8	7.7
Maximum duration treatment	20.0	18.0	20.0	18.0
Minimum duration treatment	3.0	3.0	3.0	3.0

TABLE VII  
Total Dosage

	GROUP I Sulfadiazine	GROUP II I M Penicillin	GROUP III Oral Penicillin	GROUP IV Penicillin with Sulfa Diazine Penicillin
Average total dose	39.5 g	870,000 u	4,410,000 u	45.1 g 1,212,340 u
Maximum total dose	107.0 g	2,720,000 u	14,400,000 u	94.0 g 2,720,000 u
Minimum total dose	15.0 g	400,000 u	2,100,000 u	23.0 g 420,000 u
Ratio of quantity oral penicillin to parenteral penicillin — 5.07/1				

Table VIII The most rapid decline of fever, within 24 hours or less, was noted in the patients receiving oral penicillin (Group III), 37.5 per cent. During a three day period of evaluation, complete control of fever showed a higher incidence in the patients receiving intramuscular penicillin every three hours (68.5 per cent). Oral penicillin was next in effectiveness (62.4 per cent), sulfadiazine third and combined therapy least with only 40.4 per cent response in this period of time. The duration of fever for more than 72 hours was likewise most frequently noted in Group IV (sulfadiazine plus penicillin) and least frequently noted in those receiving intramuscular penicillin and oral penicillin respectively. It is apparent from these figures that combined therapy proved to be the least effective on the febrile courses of these patients with pneumococcal pneumonias.

The mortality rates in the various groups is indicated in Tables VIII and IX. Here again combined therapy was proven to be the least effective as five deaths were recorded in the total 47 patients (10.6 per cent). Only two of these patients were over 50

TABLE VIII  
Effect of Therapy on Temperature

Duration of fever following onset of treatment	GROUP I Sulfa Per cent	GROUP II I M Penic Per cent	GROUP III Oral Penic Per cent	GROUP IV Combined Per cent
24 hours or less	25.3	33.3	37.5	6.4
24 to 48 hours	18.4	20.4	20.8	10.6
48 to 72 hours	13.8	14.8	4.1	23.4
Total becoming afebrile within 72 hours	57.5	68.5	62.4	40.4
Duration of fever more than 72 hours following onset of therapy	33.6	29.6	31.3	48.9
Expired	8.9	1.9	6.25	10.6

TABLE IX  
Mortality

GROUP I Sulfadiazine			GROUP II I M Penicillin		
Cases	Died	Per cent	Cases	Died	Per cent
90	8	8.9	54	1	1.9

TABLE IX (Continued)

GROUP III Oral Penicillin			GROUP IV Combined		
Cases	Died	Per cent	Cases	Died	Per cent
48	3	6.25	47	5	10.6

years of age, one with arteriosclerotic heart disease and the other developed a marked pleural effusion. No other associated disease were recorded in this group. The lowest mortality was 1.9 per cent in Group II receiving intramuscular penicillin every three hours. This represented the only death in 54 patients receiving this type of therapy. It occurred in a patient 54 years of age with a delay in treatment of 5 days following the onset of the disease. Three deaths were noted in the patients receiving oral penicillin with a mortality rate of 6.25 per cent. One of these was 68 years of age and another 55 years old. All three were handicapped with associated disease including bronchiectasis, generalized arteriosclerosis and severe emphysema in the first and delirium tremens with bacteremia in the second. The other had manifest evidence of malnutrition with a positive blood culture. The second largest mortality occurred in those receiving sulfadiazine (Group I). There were 8 deaths in 90 patients here, an incidence of 8.9 per cent. Only one of these patients was over 50 years of age and associated disease was present in only five.

The occurrence of complications following the onset of treatment was greatest in Group IV as indicated in Table X. Eight

TABLE X  
Complications

Group I—Sulfadiazine 90 cases	Cases	Percentage	Died
Empyema	2	2.2	2
Pleural Effusion	2	2.2	0
Toxic Hepatitis	1	1.1	0
Prerenal Azotemia	1	1.1	0
Group II—I M Penicillin 54 cases			
Empyema	2	3.7	1
Lung Abscess	1	1.9	1
Toxic Hepatitis	4	7.4	0
Group III—Oral Penicillin 48 cases			
Empyema	1	2.17	1
Pleural Effusion	3	6.25	0
Pneumococcal Meningitis	1	2.1	1
Toxic Hepatitis	1	2.1	0
Group IV—Penicillin combined with Sulfadiazine 47 cases			
Empyema	1	2.1	1
Pleural Effusion	3	6.4	0
Toxic Hepatitis	2	4.3	0
Toxic Psychosis	1	2.1	0
Prerenal Azotemia	1	2.1	0
Prerenal Azotemia	1	1.1	0

cases (17 per cent) included empyema, pleural effusion, toxic hepatitis, toxic psychosis and pre-renal azotemia. This group of patients, as was previously indicated, included the least number of patients with associated disease. Twelve and six tenths per cent of those receiving oral penicillin developed complications. In these, two deaths were recorded, one with empyema, and the other with pneumococcal meningitis. Each, however, was over 50 years of age, and was handicapped originally by bronchiectasis and chronic alcoholism with delirium tremens. Thirteen per cent of the patients in Group II developed complications and 6.6 per cent in Group I.

The duration of therapy is indicated in Table VI. This was greatest in Group IV (combined medication), averaging 7.7 days. Treatment in patients receiving intramuscular penicillin (Group IV) averaged 5.5 days and 5.8 and 6.9 days respectively with oral penicillin and sulfadiazine.

The average total dosage of chemo-therapeutic or antibiotic agents is indicated in Table VII. The quantity of intramuscular penicillin given with sulfadiazine is very close to that given alone intramuscularly. The total oral penicillin was approximately five times that of the total intramuscular penicillin. The sulfadiazine administered in Group I was less in total quantity than that combined with penicillin.

### *Discussion*

The multiplicity of studies on various modes of the use of penicillin have demonstrated effectiveness by each method. This is illustrated first by the oral route, secondly, in a study by us, by single daily massive intramuscular penicillin in peanut oil and beeswax, and thirdly, by the use of intramuscular aqueous penicillin.

Concentrations of 0.03 units of penicillin per cubic centimeter of blood controls the commoner etiological organisms producing pneumonia. This concentration is easily and readily obtained by the methods of administration which have been indicated and have been confirmed by numerous published results, and by investigators from the Hektoen Institute of Cook County Hospital. It is, therefore, reasonable to assume that a single effective agent which experimentally and clinically has demonstrated superiority over the sulfonamides, should be used alone.

There is no infection occurring in the pulmonary system in which the sulfonamides have been proven to be even the equal of penicillin. It seems, therefore, unreasonable that, unless there is a definite indication, such as the inability of the patient to accept penicillin because of hypersensitivity to this antibiotic, that

the sulfonamide should be added or substituted in the treatment. It is further unreasonable to assume that where organisms demonstrate a very high degree of penicillin resistance that they should a-priori be sulfonamide susceptible. The indications for the combined use of these two drugs at the present time would seem to be the attitude of the therapist to bring into action all of the therapeutic armamentarium which he possesses. We believe we have demonstrated this to be in error, therapeutically speaking. In analyzing the total dose of therapeutic agents used, the quantity of each, chemo or antibiotic when combined was equal to or slightly in excess of the amounts given alone. If the above reasoning were in order, some evidence should have been noted to encourage the use of this type of therapy. All aspects of clinical response which might indicate a beneficial response to combined treatment was lacking. The mortality rate was higher, the febrile course was prolonged, the incidence of complications was greater, and the duration of treatment was lengthened. All of these unfavorable results occurred in a group of patients who after analyzing them proved to be clinically less ill than those considered in the other comparative groups. These patients were subjected also to the unpredictable toxic reactions associated with the administration of the chemotherapeutic agents.

In a very few instances which we have experienced of penicillin allergy, control of this complication by anti-histamine drugs is relatively simple because of the low blood level assays of penicillin required to overcome the infection in patients invaded by the pneumococci.

Sulfonamides potentially have a much greater toxicity than penicillin. Therefore, their use must be supervised with greater caution. Fluid intake, output and urinary studies, both the reaction and the sediments must be observed frequently and carefully. Despite all of these precautions, serious complications from sulfonamide medication may occur.

Multi-medication having to be watched by the physician means additional disturbance and irritation to the patient. The increasing incidence, demonstrated by post mortem examination, not alone the lower nephron block, but interstitial sulfonamide nephritis with generalized distribution of similar allergic lesions means a much greater hazard to the patient.

Klein and Kalter<sup>7</sup> have indicated that the additional use of the sulfonamides in the body produces no increase in the penicillin titre unless both agents are present in definitely inhibitory concentration levels. The administration of a therapeutic agent on this basis seems impractical, because, as was previously indicated, the quantity of each medication as combined was equal to or

slightly greater than that used alone. Furthermore, there is no apparent need for a higher titre as the currently popular dosage has been proven more than adequate for bacteriostasis to pneumococci. Hobby and Dawson<sup>8</sup> concluded that the vastly more complex nature of the conditions which may be encountered in vivo studies over in vitro assays indicate that it is impossible to determine in advance whether or not sulfadiazine will enhance the bacteriostatic action of penicillin in human infection. The clinical evidences presented herein indicate the possibility of an antagonistic action in combined therapy rather than a synergistic activity.

### SUMMARY AND CONCLUSIONS

1) This statistical comparison readily demonstrates that penicillin is a much more superior drug than sulfadiazine in the treatment of pneumococcic pneumonia.

2) Sulfadiazine is an inferior therapeutic agent for the treatment of pneumonia as compared to the antibiotic, penicillin.

3) The evidence adduced in these series of investigations, demonstrate that in the group in which there was addition of sulfadiazine to the antibiotic therapy, there was a delayed clinical response, a greater incidence of complications, and a higher mortality.

4) The clinical use of sulfadiazine with penicillin indicates a possible antagonistic action in vivo rather than a synergistic effect.

5) There is little justification for the combined administration of the sulfonamides and penicillin in the treatment of pneumonia. Penicillin alone will accomplish the therapeutically desired goal if this is attainable.

6) There are very, very few pneumonia patients who cannot be treated with penicillin. They may require sulfonamide therapy.

### RESUMEN Y CONCLUSIONES

1) Esta comparación estadística demuestra fácilmente que la penicilina es una droga muy superior a la sulfadiazina en el tratamiento de la neumonía neumocócica.

2) La sulfadiazina, comparada con el antibiótico penicilina, es un agente terapéutico inferior en el tratamiento de la neumonía.

3) Las pruebas presentadas en estas series de investigaciones demuestran que en el grupo en el que se añadió la sulfadiazina a la terapia con el antibiótico la respuesta clínica fue demorada y hubo una mayor frecuencia de complicaciones y una mortalidad más elevada.

4) El uso clínico de la sulfadiazina con la penicilina indica una posible acción opuesta *in vivo* en vez de un efecto sinérgico

5) No se justifica la administración de las sulfonamidas y la penicilina combinadas en el tratamiento de la neumonía. La penicilina sola realiza el propósito terapéutico deseable si es posible alcanzarlo

6) Hay muy pocos pacientes con neumonía que no pueden ser tratados con penicilina. Estos casos pueden requerir la sulfonamidoterapia

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#### D I S C U S S I O N

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Washington D C

It seems to me there are two distinct parts of this subject. The first is, is penicillin better than the sulfonamides, and the second, is the combination better or worse than penicillin alone. We have treated 1250 patients with sulfonamides, all of whom had pneumococcal pneumonia, and more than 800 with penicillin. Approximately 9 per cent of the patients died when given sulfonamides,



and 45 per cent died when they were given penicillin, that is, half as many of those receiving penicillin died as compared with those receiving sulfonamides

It does not matter, apparently, what kind of penicillin one uses—at least we have not been able to demonstrate any difference between the different types, providing penicillin is used in adequate doses

Regarding the second question, as to whether the combination is better or worse than the use of penicillin alone, we cannot find any difference. Some time ago we ran a parallel series in which we used sulfadiazine on 90 patients and sulfadiazine plus penicillin on another 90 patients, and we had a case fatality rate of about one-half as great when we used penicillin plus sulfadiazine. In other words, again about 9 per cent for sulfadiazine compared with 45 per cent with the combination. I am at a loss to account for Dr. Volini's results with a seemingly greater case fatality rate in those patients who had the combination, unless it was due to the small number of patients included in his series. Because, as we know, in pneumococcal pneumonia patients who have delirium tremens or cardiac failure, or who are quite old, or who have some other complication, may die and throw the case fatality rate away over if only a small number of patients are used in the series. Dr. Volini was not able to use all his patients, because he wanted to take the entire group from one year, and yet I feel that he should continue his work into other years so that we would have a definite answer to this problem. Personally, I cannot see that the sulfonamides will cause an increase in the case fatality rate, and I feel, along with him, that we should use penicillin alone and not penicillin plus sulfonamides.

One other thing might be said. There are certain organisms infrequently the cause of pneumonia such as *Klebsiella pneumoniae* (or Friedlander's bacillus) and *Hemophilus influenzae*, which will not respond to penicillin and which will respond to sulfadiazine. In those cases the patient may be given sulfadiazine or, better still, sulfadiazine plus streptomycin. The practical compromise we have evolved is to collect a specimen of sputum from every patient as soon as the diagnosis, or tentative diagnosis, of pneumococcal pneumonia is made and put it in the refrigerator. We have found that typing after three or four days is just as good on those specimens as on fresh specimens. Then if the patient does not do well in 48 hours, sulfadiazine may be added tentatively, typing of the sputum may be done, and cultures made. Then you can see whether you have a type of pneumonia which needs other therapy, namely, sulfadiazine plus streptomycin. I hope Dr. Volini will continue his work.

*Closing Remarks*

*Italo F Volini, M.D., F.C.C.P.* I wish to thank Dr Dowling for his remarks and most assuredly we shall continue this line of investigation I would like to call to mind the time when we were using rabbit serum When the sulfonamides were introduced, I think we first called attention to the fact that the combination therapy of immune rabbit serum and the sulfonamides produced a greater mortality than where sulfonamides were used alone That, in fact, prompted this study It was a small group of patients in which I demonstrated these results and it was not until the Pneumonia Control Commission of Pennsylvania evaluated their statistics in a large group of cases, that we were able to find out conclusively that such a combination was not as satisfactory as the use of sulfonamides alone

The re-administration of sulfonamide therapy after an intermission is probably a very important factor in the sensitization of patients to sulfonamides Very frequently we have been unable to obtain a history of previous sulfonamide administration until the patient manifests serious toxic signs The indications for sulfonamide therapy today I believe are greatly restricted and I think are becoming more and more so, due to the availability of penicillin and as Dr Dowling mentioned, streptomycin, which will take care of many of these resistant organisms that do not respond to penicillin, and against which streptomycin is a better agent than is sulfonamide Sulfonamide medication today can be pushed down to very few indications, in my opinion Since I have seen so many of these individuals demonstrating the serious toxic manifestations of lower nephron block and of interstitial nephritis at the postmortem table—those general allergic findings which are comparable to the investigations of Rich at Johns Hopkins in his sensitization studies—we have felt that the sulfonamides can be restricted to use in the meningitides, due particularly to the meningococcus, pneumococcus and other pyogenic cocci However, many of these must receive penicillin by parenteral injections In the pre- and postoperative care of patients selected for surgery of the bowel, the unabsorbable types of sulfonamide are particularly useful In cases of bacillus dysentery infection, in some cases of lymphogranuloma venereum, they are useful Thus there are relatively few indications today for the use of sulfonamides, due to the introduction of the antibiotics, penicillin and streptomycin

# Chronic Nontuberculous Pulmonary Infections and Their Sequelae\*

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## FORWORD

The role of chronic nontuberculous infections as a cause of human misery and disability has not been adequately appreciated. The initial, causative factor, primarily seemingly insignificant and justifying scant consideration, may eventually pass through a series of conditions, leading in the end to invalidism and even death. It is my purpose in this paper briefly to sketch the course of chronic nontuberculous infections from the beginning through their progressive stages to their end results, such as, pulmonary fibrosis, cavitation, and bronchiectasis.

It is impossible to deal separately and fully with each of the etiologic agents involved in these infections, but reference will be made to the role of chronic lobar and chronic bronchopneumonia, aspiration pneumonitis, atelectasis, pneumoconiosis, bronchial and bronchiolar stenosis, metastatic lung infections, the mycoses and syphilis, as well as the milder, but quite important, chronic infections of the nasopharynx and bronchi. It is necessary to stress the role in the initial development of these chronic infections of such conditions as acute nasosinusitis, subacute bronchitis, and the acute pneumonias. A closer cooperative understanding between the nose and throat specialist and the general practitioner would be helpful in diagnosing and eradicating suppurative conditions of the nasal sinuses. These infections are often given palliative treatment, only to recur each winter, until a chronic bronchitis and eventually a chronic pneumonitis and bronchiectasis may develop. The dreadful end results could be, in many cases, obviated in the beginning by prompt treatment, and by carefully following the patients through to a cure. Patients following attacks of acute pneumonia should be regularly checked for the presence of residual foci of infection in their lungs, small atelectatic areas, single or multiple, small bronchopneumonic areas, and slight abscesses, may be found to reward us for our diligence.

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### *Bacteriology*

The bacteriology of chronic nontuberculous pulmonary infections, is well worth considering Petroff and Schwartz<sup>1</sup> in an excellent study have stressed that the bacteriology of chronic nontuberculous pulmonary infections has not kept apace with other methods for diagnosis They discuss the bacteriology of these pulmonary infections by studying three types, namely, lung abscess and gangrene, bronchiectasis, and pulmonary infections which simulate pulmonary tuberculosis or at times may occur in symbiosis with tuberculosis They state that abscess of the lung is not due to a specific micro-organism but is the result of various types, differing as to the kind of abscess found, anaerobic bacteria, such as vibrios, anaerobic streptococci, and fusospirochetal organisms especially being the main causative factors in producing putrid lung abscess and gangrene, aerobic, nonputrid, lung abscess having the pyogenic bacteria, diplococcus pneumoniae, Hemophilus influenzae, Neisseria catarrhalis, diphtheroids, streptococci and especially staphylococci predominating, mycotic suppurative processes, frequently simulating tuberculosis, may be caused by actinomyces, moniliae, aspergilli, penicillia, and coccidiodes, and to a lesser extent by many other fungi, especially of the fungi imperfecti group It is understood that tubercle bacilli are always absent in the sputum of these patients

### *Etiologic Diseases*

Although some of these patients may present an acute, and at times a stormy onset, the process develops more gradually in a large percentage of them A simple bronchitis, following an acute nasopharyngeal infection, for instance, may lead to an extension of the infection into the wall of the bronchi with areas of pneumonitis resulting The general health of the patient may be practically unimpaired, although there may be a tendency during exacerbations to increased cough and some fever The majority are in full adult life The period of increased symptoms is usually during the colder, winter months Cough and expectoration may be the only symptoms, although fever, pleurisy, and even hemoptysis may occur The lesions are ordinarily in the lower lobes, especially the left It is interesting to recall that with the recurring exacerbations the physical findings have a marked tendency to recur in their original location The similarity of the clinical findings to early pulmonary tuberculosis is striking, but the distinction between the two entities is aided by the basal location of the physical and roentgenologic findings in the nontuberculous individual, in contradistinction to the upper lobar findings in the

tuberculous patient. It is possible the pathology in these cases may be a localized bronchitis with lobar or lobular distribution involving the submucous and peribronchial tissues. This condition may clear up after an attack and recur at a later date, or persist in a latent subacute form. In this latter case, the acute recurrences affect the original site and are probably due to a localized lesion. This may lead into chronic interstitial pneumonia or bronchiectasis. It is my opinion that these recurring episodes are due, not to new acute infections, but to recrudescences of the same infection which has been lying dormant in the lungs during the interium between flare-ups.

It has been indicated heretofore that conditions other than described in the proceeding paragraph may be operative in producing chronic nontuberculous pulmonary infections. Some consideration of these conditions will be mentioned.

### *Pulmonary Abscess and Gangrene*

Pulmonary abscess and gangrene<sup>2,3</sup> may follow aspiration of foreign material after surgical operations, pneumonia, wounds to the lungs, the presence of carcinoma of the bronchus, lung or esophagus, and rare infections such as mycoses, cysts or the extension of suppuration from beneath the diaphragm, liver or perirenal tissues. They are not specific diseases because they are due to a wide array of bacteria. Bucher<sup>4</sup> in a study of the pus obtained bronchoscopically in 118 cases of pulmonary abscess found 18 different organisms, with the streptococcus (hemolyticus, viridans, nonhemolyticus), micrococcus catarrhalis, pneumococcus, bacillus influenzae, staphylococcus albus and aureus, diphtheroid bacilli, spirochetes, fusiform bacilli and the micrococcus tetragenes predominating. Rona<sup>5</sup> in 1905 first recognized fusiform bacilli in pulmonary gangrene. Oliver and Wherry<sup>6</sup> in 1921 first described the bacterium melaninogenicum, and since that time this strictly anaerobic, non-motile, polymorphic and gram-negative organism in symbiosis with other bacteria has been shown to produce extensive tissue necrosis in the lung. Unless this acute process heals, a chronic abscess associated with bronchiectasis may ensue.

### *Chronic Lobar and Bronchopneumonia*

Especially after influenza, measles and whooping cough, an acute broncho-pneumonia may be followed by a chronic progressive pneumonitis, or the development of atelectasis and bronchiectasis. In some cases of lobar pneumonia resolution of the lung tissue may not occur promptly, and rarely abscesses may be followed by cavitation, or another group may develop a chronic course through

many months or years. We have seen a case of acute Friedlander's bacillus pneumonia assume a chronic form which lasted for years, and closely resemble the clinical picture of chronic tuberculosis.

#### *Aspiration Pneumonitis*

The aspiration of foreign bodies, especially those of an organic nature, may give rise to bronchial and peribronchial inflammation and suppuration, usually in the hilar or midportions of the lungs. It is clear that these unfortunate conditions may be obviated only by making roentgenograms at once when there is a likelihood of a child aspirating any foreign material.

#### *Atelectasis*

Atelectatic areas, occurring in infants at birth, or from massive collapse following operations in any age group, may become infected, at first the bronchial and bronchiolar mucous membranes are involved, later the infection may spread to the peribronchial tissues. A focus for subsequent exacerbations of infection may follow, and be erroneously termed "bronchitis," or, if the recurring attacks of acute pneumonitis be more severe, they may be diagnosed "pneumonia." As time passes on, a chronic recurring, localized pneumonitis develops and may last for many years.

#### *Bronchial and Bronchiolar Stenosis*

It is well recognized that the occlusion of the bronchi or bronchiole may precipitate the development of atelectatic areas distal to the obstruction, and that a chronic pneumonitis may develop with either bronchiectasis or pulmonary abscess occurring, singly or together. An inflammatory condition of a bronchus, a benign or malignant bronchiogenic tumor may be the etiologic agent.

#### *Metastatic Lung Infections*

A chronic, relatively mild pulmonary infection may follow metastatic pulmonary emboli. The clinical picture will vary according to whether the emboli are large, or small and numerous, a serious localized abscess may follow a large embolus, whereas small, multiple emboli may rarely produce a chronic recurring pneumonitis.

#### *Pneumonoconiosis*

Workers on sandstone and quartz, or any combination of large amount of silica, frequently suffer from chronic pneumonitis and nodular pulmonary fibrosis often follows.

#### *Syphilis*

Many years ago in a study<sup>7</sup> of the incidence of syphilis in the Houston Anti-tuberculosis Clinic, I was impressed with the belief

that pulmonary syphilis is more frequent than is commonly believed to be true. About 1 in 250 cases, previously diagnosed as tuberculosis, was believed to have pulmonary syphilis. The patients were largely drawn from Negro and Mexican admissions. Single or multiple gummas were noted, as well as definite fibrotic streaking and thickening of the bronchial and peribronchial tissues.

### *Mycoses*

Meakins<sup>8</sup> lists four mycotic diseases of the lungs, namely, blastomycosis, actinomycosis, streptothricosis, and aspergillosis. The term blastomycosis is used in a general sense, meaning the various fungi reproducing by blastospores, the so-called "yeast-like" fungi—the cryptococcus, monilia, torula and oidium. Actinomycosis and streptothricosis may be classified under the nocardia, and distinguished by the fact that a case of streptothricosis has no granules in the sputum and actinomycosis has. Aspergillosis is a very chronic disease and runs a mild course. We have previously stressed the insidiousness and latency of mycotic infections of the lungs. The clinical course of these invasions may be quite similar to chronic fibrosing pulmonary tuberculosis. The diagnosis may be difficult, and should never be made from the expectorated sputum alone. In a personal study<sup>9</sup> of 301 patients, fungi were isolated from the expectorated sputum in 45 patients, in 18 patients (6 per cent) we isolated fungi from tracheal washings. We considered the other 27 fungi contaminants and pathogenic, the saprophytic fungi were of the following genera: cryptococcus Kutzinger, monilia Persoon, sporotrichum Link, acremonium Link, saccharomyces Meyen, and aspergillus Michel. The saccharomyces, constituting 64 per cent of the fungi classed as contaminants, were consistently saprophytic and parasitic. There were 5 cases of pure mycoses, identified as 1 aspergillus fumigatus, 1 cryptococcus hominis Vuillemin, and 3 sporotrichum Schenck, an incidence of 1 to 60 mycotic to tuberculous patients. Although fungous infections, occurring as single entities, usually run a benign, but protracted course, we believe fungi, when associated with tuberculosis, enhances the activity of the tuberculous process.

### *Classification*

Chronic nontuberculous pulmonary disease may be classified on an anatomical and pathological basis according to the following table,<sup>10</sup>

#### I Bronchial Tube Disease

##### A Reactive injury

- 1 Mucous membrane—reaction "catarrhal bronchitis"
- 2 Bronchial wall—reaction "mural bronchitis"

**B Traumatic injury**

- 1 Bronchial obstruction
- 2 Bronchial dilatation

**II Air Cell Disease****A Reactive injury**

- 1 Pneumonia
  - a Inflammatory
  - b Organized

**B Traumatic injury**

- 1 Pulmonary collapse (atelectasis)
- 2 Pulmonary over-expansion
  - a Diffuse (emphysema)
  - b Localized (pneumectomy)

There is a type of bronchitis, which Andrus<sup>11 12 13</sup> terms idiopathic, occurring in a large group of people, characterized by chronic cough and expectoration, which does not result in a chronic pneumonia, fibrosis, bronchiectasis, etc. This is the so-called "catarrhal bronchitis." There is a similar group showing in the radiographs some thickening of the bronchial tree, due to reactive changes in the bronchial walls. This is the "mural bronchitis" of the previously listed table, and the bronchial wall reaction is a postpneumonic type of injury. The radiographic shadows in mural bronchitis may be due, however, to an arteriosclerotic process. It has been shown from Robinson's<sup>14</sup> studies on surgically removed bronchiectatic lobes that the infection probably passes from inside the bronchial wall, rather than from within the lumen of the bronchi, because he found normal mucous membrane and functioning cilia in the bronchi in such cases. We may, then, have two distinct types, catarrhal bronchitis (x-ray negative), mural bronchitis (vascular, infectious) (x-ray positive). Traumatic injury to the bronchi may be due to either, or both, obstruction or dilatation of the tube. The presence of a major area of atelectasis indicates obstruction of one of the larger bronchi, smaller, patchy atelectatic areas the result of a bronchiolar stenosis as may be found in bronchopneumonia.

Chronic disease of the alveolar air cells may be caused by either inflammatory or traumatic injury. There may be a shrinkage or an overexpansion of the pulmonary tissues. Pulmonary shrinkage caused by contraction of scar tissues, may be extensive or "patchy" in distribution. It should be stressed that postpneumonic lung shrinkage is more likely to be caused by pulmonary collapse than to fibrosis, although fibrosis usually follows atelectatic collapse. The primary underlying factor in the production of chronicity in nontuberculous lung disease is atelectasis. Pulmonary overexpan-



sion is a compensatory mechanism, when the volume of the chest contents is reduced by localized shrinkage, or the capacity of the thoracic cage is increased by outward displacement of the chest walls. The overexpansion may be diffuse or localized. The localized type is due to an infection with a persisting chronic patchy atelectasis, and consists of localized emphysematous air blebs. Andrus calls this latter condition "pulmonectasis," and a chronic infection and overdistension of the pulmonary bases, formerly listed as unresolved pneumonia, chronic basal disease, pneumonitis and bronchiectasis—suspect could fall in this category.

### *B End Results*

It has been suggested by Miller<sup>15</sup> that bronchiectasis is of congenital origin, but the wide consensus of opinion is that a congenital origin is doubtful. In my opinion the secondary factors, bronchial obstruction and atelectasis, with an infection following such a mechanical obstruction, seems more plausible as etiologic factors in a preponderant percentage of cases. It must be added, however, that congenital bronchiectasis may occur, although we are not especially concerned with a discussion of the congenital type in this paper. Ballou and Ballou<sup>16</sup> have classified five types of bronchiectasis, based on iodized oil injections, as follows: grape, clubbing, cylindrical, saccular, and bead formation. The symptomatology may be quite varied, in fact lacking in early cases, and consist only of the subjective and objective signs of the primary causative disease. As time runs on, the clinical picture gradually changes, and new added symptoms come into prominence. Cough and expectoration may be the only distinct symptoms. The cough may be hacking, persistent or severe, dry or productive. The inhalation of substances, such as tobacco smoke or gases, may be very irritating. The sputum<sup>17</sup> contains a large amount of water and albumin, peptones, amino acid, pus and bacteria, it usually has a foul odor, and may exceed 1000-15000 cc in 24 hours, being expectorated more or less persistently, or more usually, paroxysmally. The sputum, ordinarily but not regularly, separates after expectoration into three or four layers, a pale greenish-yellow layer of air bubbles, mucus and pus, a mid-layer of pus cells, fat rests, Dittrich's plugs, and detritus. The foul odor of the sputum may be distressing to the patient and as previously stated is due to the presence of anaerobic organisms. More advanced cases of bronchiectasis may have fever, sweats and chills. These episodes are due to attacks of recurring pneumonitis and not to retained intrabronchial secretions. It follows, therefore, that fever may continue, even though the bronchial secretions are expectorated. Especially in cases of numerous smaller bronchial or bronchiolar

dilatations it must be assumed that pneumonitis is present when toxic manifestations, fever and sweats, are present. Hemoptysis is frequently noted. Joint pains may also be associated. The physical findings are not typical, although they are usually basal in location, in contradistinction to the findings in tuberculosis, which are more likely to be apical. There may be increased voice conduction (pectoriloquy) or decreased breath sounds, and most always rales. Signs of localized atelectasis or even cavitation may be present. There is usually a moderate, secondary type of anemia and some polymorphonuclear leucocytosis. The organisms in the sputum consist of the great array previously discussed. The diagnosis, although to be strongly inferred from the history, symptoms and physical findings, is not complete without iodized oil injection. The normal primary and secondary divisions of the bronchi do not cast a radiographic shadow, and although a diseased bronchus does cast a shadow, it is very difficult to decide whether the shadow is due to the bronchus itself, or to a peribronchial pathology. Therefore, for exact diagnosis of bronchiectasis, iodized oil injection is essential. Bronchoscopy is of great help in that obstructive new growths in stenotic conditions may be found, the discharging pus may be localized, the iodized oil injection may be more accurately made, and uncontaminated cultures may be obtained. Singer<sup>18</sup> has stated that a diagnostic pneumothorax may reveal a bronchiectatic, atelectatic lobe, hidden in the cardiac shadow. It is my opinion that advanced bronchiectasis is incurable by the ordinary remedial agents, although they may be definitely palliative. The disease is characterized by remissions, and it is difficult to judge the value of rest, climate, postural drainage, vaccine, drug therapy, or local treatment, such as direct intra-bronchial application of drugs, bronchial lavage and inhalations.

Considerable pulmonary fibrosis, with chronic pneumonia and abscess formation, may be expected to be found in many, if not most, cases of definite bronchiectasis. It has been shown that an exudate in the alveoli of the lungs may become vascularized and fibroblasts and capillaries, with the formation of connective tissue, ensues. Scar tissue will ultimately distort the bronchi and make emptying impossible. The added presence of pneumonic patches and fibrinous pleuritis, resulting in parenchymal fibrosis and adherent pleura, respectively, further distort the bronchi and the pulmonary tissues and the chest cage. Chronic abscesses may form in the resulting atelectatic areas, these may empty periodically through the bronchus, or, when they are numerous and small, may remain as purulent foci within the lung tissues.

The ultimate fate of these patients depends upon the type and prominence of the bronchiectatic process, and the extent of com-

plicating factors, such as pulmonary fibrosis and recurring pneumonitis, abscesses, the presence of scar tissue, the degree of intrathoracic distortion of the heart and mediastinal contents, and the associated cardiovascular and toxic phenomena. Severe cases may die in a relatively short time from fulminating hemoptyses, acute pneumonia or abscess, or they may survive many years. Eventually the latter cases die from a severe recrudescence of the bronchiectatic and associated conditions, or from the more gradual development of cardiac failure, amyloidosis, or general nutritional failure from chronic toxemia.

### SUMMARY

It should be evident from this review that the early treatment and eradication of acute and subacute disease entities within the respiratory system, is positively necessary if we are to expect to obviate their serious sequelae. The best treatment is, therefore, preventive, and little may be expected from medical measures after these chronic infections have become evident. It is the main and primary object of this discussion of chronic nontuberculous infections of the lungs to stress the urgent necessity of diagnosing the earliest etiologic pathologic states, which lead otherwise to an incurable and serious disease, and, do all in our power to promote, if possible, their prompt and thorough eradication.

### RESUMEN

Este repaso debe hacer evidente que el tratamiento temprano y la erradicación de las enfermedades agudas y subagudas del sistema respiratorio son absolutamente necesarios si hemos de abrigar esperanzas de evitar sus graves secuelas. El mejor tratamiento es, por consiguiente, profiláctico, y poco se puede esperar de medidas médicas cuando estas infecciones crónicas han llegado a ser evidentes. El objeto principal y primario de esta discusión de infecciones no tuberculosas crónicas de los pulmones es recalcar la necesidad urgente de diagnosticar los estados patológicos que las anteceden, los que de otra manera conducen a una grave e incurable enfermedad, y de usar todos nuestros esfuerzos para lograr, si es posible, su erradicación pronta y completa.

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# The Measurement of the Function of the Lungs\*

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The measurement and evaluation of pulmonary function has been a difficult procedure. The common approach to this problem has been the crude method of judging pulmonary function by noting whether a subject shows evidence of dyspnea after exercise (walking up and down a ward or up a flight of stairs). This method is still the most frequent one employed in the majority of institutions where there is a need of knowing the capability of lung function.

The measurement of vital capacity is used in many places for determining pulmonary function. This method denotes only one phase of lung function, namely the ventilatory one. It is the function of bringing sufficient air into the lungs for diffusion of oxygen through the alveolar membranes into the alveolar capillary bed. This measurement of the ventilatory process does not therefore foretell the ability of the alveoli to diffuse oxygen into the pulmonary capillaries and carbon dioxide out of the capillaries into the alveolar spaces. There is therefore another phase of pulmonary function—a diffusion one. Pulmonary function therefore depends upon both a ventilatory and a diffusion phase. Before discussing methods of determining lung ventilation and diffusion of oxygen and carbon dioxide it would be logical to review some new concepts in lung ventilation and diffusion of gases in the pulmonary alveoli.

Orinstein, Heiman, Friedman and Friedlander<sup>1</sup> stated, after investigating 170 subjects with impaired lungs, that the capability of the lungs to ventilate had no relationship to their capability to diffuse oxygen and carbon dioxide, that when ventilation was in the normal range, diffusion was usually good and only occasionally was ventilation good and diffusion poor. On the other hand, when ventilation was impaired the diffusion of oxygen and carbon dioxide had no relationship to the reduced ventilation. The above authors further stated that in subjects with marked impaired lungs and with great reduction in ventilation, diffusion of oxygen and carbon dioxide could be on a normal level. They further state the impaired lung tissues take little or no part in the ventilation and the movement of air in the lung by-passes

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the impaired tissues and only ventilates the normal alveoli. The normal alveoli only being ventilated it is understandable to have normal diffusion of oxygen and carbon dioxide. These authors compare the expansion of the lungs to two balloons connected by means of a Y tube in a negative pressure chamber. The balloons being of equal tensile strength and the stem of the Y tube open to the atmosphere, the balloons expand equally. If the tensile strength varies the balloon with the least strength expands while the one with the greater tensile strength remains slightly distended (Fig 1). They state that impaired lung tissue has greater tensile strength than normal lung tissue and in a similar manner does not expand while the normal lung with the lesser tensile strength is ventilated. The size of the lumen of the bronchus also plays a role in ventilation. When the lumen of the bronchus is narrowed, less air enters that portion of the lung. This is especially true when two lungs compete for air through the trachea. These same authors suggest blowing through the stem of a Y glass tube with the lumen of one of the arms narrowed. The arms are

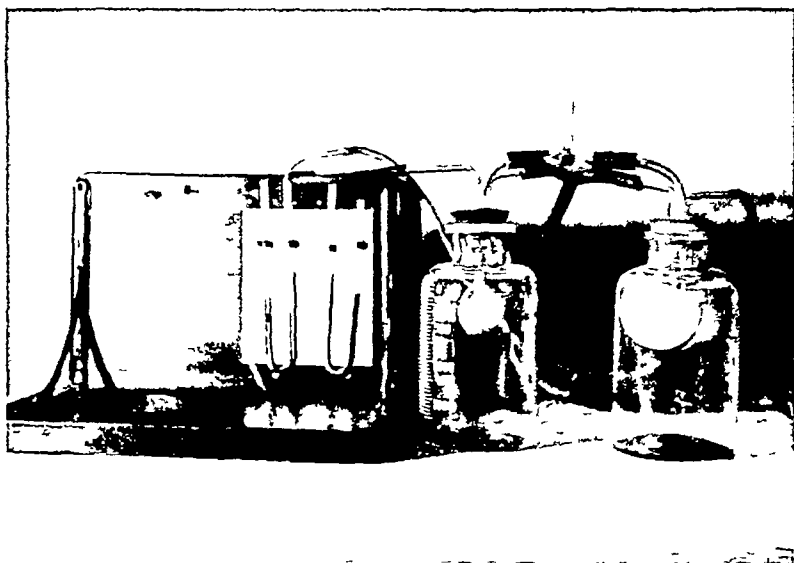


FIGURE 1 Two balloons of slightly unequal tensile strength are placed in two bottles and connected to the arms of a T tube the vertical part of the tube being open to the atmosphere. Each flask is connected to a mercury manometer so that the negative pressure of the bottles can be measured. Through a separate opening in the rubber stopper of each bottle a tube is inserted and joined to each arm of a T tube. The negative pressure is produced with a suction hand pump through the stem tube. The pressure in each bottle is the same as can be seen by the mercury manometer. The balloon of the least tensile strength enlarges whereas the one with the greatest tensile strength remains slightly distended.

to be placed in a beaker of water about 1 cm below the surface. When one gently blows through the stem the air will be seen to come through the non-narrowed arm as bubbles and only an occasional one emerges through the narrowed arm. This phenomenon may be observed in patients when one of the major bronchi is partly obstructed. The air easily enters the major bronchus of the contralateral lung and distends the lung. The lung in which the lumen of the major bronchus is narrowed receives little air and expands poorly. The normal lung thus over-expands and the mediastinum shifts towards the involved lung. In expiration the reverse takes place, air rapidly flows out of the normal lung and escapes with difficulty from the involved lung which now appears to be larger than the normal one. The mediastinum shifts to the opposite side.

The bronchial tree divides in a similar manner to the trachea so that each lobule of the lung competes for air through a stem bronchiole. Therefore, besides the question of tensile strength of the impaired lung the effect of pulmonary disease on the architecture of the bronchial tree is also a factor in aeration. Ornstein, Heiman, Friedman and Friedlander<sup>1</sup> did some interesting experimental work with balloons attached to a glass Y tube in which one arm of the Y tube had partially obstructed and the balloons placed in a negative pressure chamber. They found that the balloon with the lesser tensile strength would expand even when it was attached to the narrowed arm of the Y tube. From the above they assumed that the most important factor in ventilation of lung tissue is the tensile strength of the lung and the tensile strength of lung tissue is a much greater factor than changes in the lumen of the bronchi. Both lungs apparently compete for the air flowing down the trachea and the lung with least tensile strength obtains almost all of the air. When both lungs are of the same tensile strength air flows into both lungs. The impression of this group of authors is that even in lungs which may be considerably impaired the normal pulmonary tissue in both impaired lungs will be ventilated and will diffuse oxygen and carbon dioxide in a normal range (Fig 2).

### *Pulmonary Ventilation*

Pulmonary ventilation is an important phase of lung function and on its efficiency the comfort of the individual depends a great deal. The simplest ventilatory test is the measuring of the vital capacity by means of a spirometer and comparing the result obtained with the calculated vital capacity from charts based on the standing height standard, the surface area standard and the weight standard.

### *Ventilatory Tests*

Knowing the actual vital capacity and the calculated normal vital capacity, the maximum minute ventilation of the subject on maximum effort may be predicted Sturgis, Peabody, Francis Hall and Fremont-Smith<sup>2</sup> have studied the actual minute ventilation in a group of 12 young normal men They found that these young normal men had a maximum minute ventilation of twelve times the resting minute ventilation when they rode a stationary bicycle until they were forced to stop because of complete exhaustion During the last one and a half minutes of the ride when the exercise was most violent and the dyspnea great, the average minute ventilation of air they breathed was 60.5 liter or about twelve times the amount of air they breathed when they were lying down and at complete rest Sturgis and his group also noted, when the maximum minute ventilation was reduced to six times the resting minute ventilation, the 12 young men could walk on level ground without any dyspnea With this reduction in the minute ventilation, any effort of exertion, such as climbing stairs, induced symptoms of dyspnea The dyspnea further increased as the maximum minute ventilation was decreased Sturgis et al worked out a formula to predict the maximum minute ventilation which was sufficiently close to the actual results obtained in their experiments The formula is as follows

$$\frac{\text{Actual vital capacity} \times 35}{3} = \text{Predicted maximum minute ventilation at maximum exertion}$$

In the above formula 35 represents the average respiratory rate during the last one and a half minutes of violent exercise The numeral 3, the denominator, represents the depth of inspiration as being one-third of the vital capacity through this last one and a half minutes of violent exercise

Kaltreider and McCann<sup>3</sup> confirmed the above observations of Sturgis and his co-workers The former investigations present a formula which they state is closer to the actual maximum minute ventilation The Kaltreider and McCann formula is as follows

$$\frac{41 \times \text{actual vital capacity} \times 37}{100} = \text{Predicted maximum minute ventilation at maximum exertion}$$

Ornstein and Epstein<sup>4</sup> worked out a formula utilizing the actual vital capacity and calculated normal vital capacity of the subject based on the investigation of Sturgis et al and Kaltreider and McCann, which also predicted the maximum minute ventilation on maximum exertion Ornstein and Epstein assumed that the average normal person's maximum minute ventilation on maxi-



maximum exertion was ten times the resting minute ventilation. The formula is as follows:

Maximum minute ventilation on maximum exertion based on actual vital capacity  $\times$  Maximum minute ventilation on maximum exertion based on calculated normal vital capacity 10

X equals the number of times the maximum minute ventilation on maximum effort is greater than the resting minute ventilation. The formula may be reduced simply to

$\frac{\text{Actual vital capacity} \times 10}{\text{Calculated normal vital capacity}}$	=	The number of times the maximum minute ventilation on maximum exertion is greater than the resting minute ventilation
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The latter authors found that when the predicted maximum ventilation on maximum exertion was no lower than 6 times the resting minute ventilation there usually were no symptoms of dyspnea. Below the above level symptoms of dyspnea increased proportionally.

Hermannsen<sup>5</sup> described a method of measuring pulmonary ventilation in which the subject was connected to a spirometer and was allowed to breathe into it normally for a few minutes to become adjusted to the new condition of breathing and then was made to breathe at maximum capacity as deeply and rapidly as possible for thirty seconds. This maximum breathing capacity was recorded on a drum. A Tissot spirometer could be used or a Douglas bag and the accumulated gas in the bag measured through a gasometer. Cournard, Richards and Darling<sup>6</sup> established the following standards for the maximum breathing capacity: the mean value for males 154 liters per minute and for females 100 liters per minute. By determining the resting minute ventilation and the maximum breathing capacity a good concept of lung ventilation can be made. Divide the resting minute ventilation result into the result of the maximum breathing capacity. The figure obtained will be the actual number of times an individual could ventilate in a minute above that of the resting minute ventilation. The above has been called the "Ventilatory Reserve." Assuming that 7.5 liters would be the average resting minute ventilation in the normal male with a maximum breathing capacity of 154 liters, the normal ventilatory reserve would be 20 and in the normal female the ventilatory reserve would be 13. The ventilatory reserve is a very capable measurement of pulmonary function because it is based on the resting minute ventilation (which the author finds very variable from 4 to 10 liters and very constant to each individual) and the maximum breathing capacity. If the resting minute ventilation was 5 liters in one

male and 10 liters in another but the maximum breathing capacity in both were 100 liters, in the first male the ventilatory reserve would be normal (20), and in the second male would be diminished (10)

The author has found this method of estimating lung function best and much more satisfactory and accurate than the use of the vital capacity with the prediction of the maximum ventilation on maximum exertion (See Table 1)

### *Pulmonary Diffusion*

In 1946 Ornstein, Herman, Friedman and Friedlander<sup>1</sup> published a new method for the measurement of oxygen and carbon dioxide diffusion in the lungs. The above authors demonstrated that following a standard exercise test in which thirty steps are taken in a minute, normal males when connected with a rebreathing bag containing a liter of air would absorb a good portion of the oxygen in the rebreathing bag, leaving an oxygen residue of about 7.95 ( $\pm 0.851$ ) volumes per cent. The carbon dioxide would increase to about 8 ( $\pm 0.436$ ) volumes per cent. The above figures were the mean values in 23 normal males. In 23 normal males the oxygen volumes per cent varied from a low of 6.84 to a high of 9.5. The mean volume per cent of oxygen found in the rebreathing bag after 20 seconds following a similar standard exercise test in 25 normal females was 8.30 ( $\pm 0.74$ ) volume per cent. The average increase in carbon dioxide was 7.70 volume per cent ( $\pm 0.497$ ).

In utilizing this method of measuring alveolar permeability, the finding of an oxygen volume per cent up to 9.5 was considered good diffusion; any volume per cent lower, very good. A volume per cent above 10 was an indication of impairment of permeability and diffusion.

### *Method of estimating diffusion of oxygen and carbon dioxide*

The method was planned after the manner Plesch<sup>7</sup> used in determining venous carbon dioxide. A rubber rebreathing bag was fitted to a three-way valve. The rubber mouth piece was attached to a tube which communicated with the room atmosphere. A turn of the three-way cock connected the tube with the rebreathing bag. There is a tube leading to the rebreathing bag for the removal of samples of air.

### *Rebreathing Bag Assembly*

#### *Parts*

- A) Mouthpiece on one arm of a three-way stopcock (Fig. 3)
- B) Second arm of three-way stopcock through which the patient breathes room air during exercise period

TABLE 1

The patients appearing in this study fall into two groups, those who came to consult because of dyspnoea and those upon whom pulmonary function tests were performed in order to determine the feasibility of thoracic surgery. This table only concerns the ventilatory function.

			Age in Sex years	Diagnosis	Dyspnoea	VENTILATORY FUNCTION			
						V C per cent	R M V Liters	M B C Liters	V R
1	W	M	48	Pulmonary tuberc	+	59	8 09	41 60	5 2
2	W	M	49	Pulmonary tuberc	+	38	6 20	47 60	7 5
3	W	M	37	Pulmonary tuberc	+	42	7 00	36 30	5 2
4	W	F	44	Pulmonary tuberc	O	75	5 39	60 2	11 2
5	W	M	54	Pulmonary tuberc	O	58	5 49	74 5	13 6
6	W	M	50	Pulmonary tuberc	+	60	7 00	25 7	3 7
7	W	F	37	Pneumonectomy Congenital cystic dis, left lung	O	59	4 40	49 5	11 2
8	W	M	60	Pulmonary tuberc Asthma Bronchiectasis	+	34	6 67	28 2	4 2
9	W	M	48	Pulmonary tuberc	+	53	6 90	27 6	4 0
10	W	M	55	Bullae Pulmonary tuberc	+	55	6 87	29 9	4 3
11	W	M	60	Asthma	+	51 5	4 98	20 4	4 1
12	W	M	59	Silicosis	O	69	8 50	68 0	7 9
13	W	M	57	Pulmonary tuberc	+	58	6 98	31 3	4 5
14	W	M	47	Bronchogenic carcinoma Trumpeter	O	90	6 55	59 0	9 0
15	W	M	58	Asthma Bronchiectasis Bullae, Emphysema	+	77	6 32	42 8	6 8
16	W	M	53	Pulmonary tuberc Thoracoplasty Emphysema	+	47	6 87	14 49	2 1
17	W	M	48	Asthma, Emphysema	+		7 99	44 3	5 5
18	W	M	52	Bullae	+		5 79	26 1	4 5
19	W	M	50	Chlorine Gas poisoning	+	78	8 72	49 4	5 7
20	W	M	50	Emphysema	+	65	6 74	62 0	9 2
21	W	M	43	Pulmonary tuberc	+	75	5 72	68 0	11 9
22	W	M	56	Hodgkin's disease Emphysema	+	85	9 02	51 2	5 7
23	W	M	57	Cystic lung Emphysema	+	59	7 36	28 4	3 9
24	W	M	53	Bullae Bronchiectasis Chronic asthma	+	41	5 94	14 3	2 4

TABLE 1 (Continued)

Age in Sex years				Diagnosis	Dyspnoea	VENTILATORY FUNCTION			
						V C per cent	R M V Liters	M B C Liters	V R
25	W	F	21	Pulmonary tuberc	O	47	5.91	63.4	10.7
26	W	M	57	Silicosis	+	78	6.90	89.0	8.8
27	W	M	64	Emphysema	+	47	7.03	20.9	2.97
28	W	M	59	Emphysema	+	76	9.25	43.1	4.7
29	W	M	34	Bullae	+	71	6.71	27.4	4.1
30	W	M	35	Lung mass	+	29	6.64	23.1	3.5
31	W	M	72	Pulmonary tuberc	O	71	8.01	66.2	7.29
32	W	M	48	Thoracic injury Asthma	+	45	7.97	50.6	6.4
33	W	M	70	Asthma Bronchiectasis	+	62	8.00	64.0	8.0
34	W	M	52	Emphysema Asthma	+	51	7.6	25.0	3.3
35	W	M	24	Pulmonary tuberc	O	40	6.4	62.1	9.7
36	W	F	60	Adenoma of right lung	O	83	5.01	52.3	10.4
37	W	M	32	Reexpanded bilateral pneumothorax	O	74	6.35	88.0	13.9
38	W	M	53	Bronchiectasis	+	73	7.98	64.0	8.0
39	W	F	29	Pneumonectomy (tuberc)	O	49	5.96	44.6	7.5
40	W	M	68	Bronchogenic carcinoma	+	97	6.65	76.8	11.5
41	W	M	21	Industrial dust case	+	76	6.49	83.1	12.8
42	W	F	38	Pneumonectomy (tuberc)	O	39	6.30	48.0	7.7
43	W	F	53	Over-weight	O	98	4.75	93.6	19.7
44	W	M		Magenblase, Cough Expectoration	O	64	5.50	67.5	12.3
45	W	M	42	Lobectomy, left upper lobe (tuberc)	O	90	6.75	107.7	16.0
46	W	F		Cardiac Rheumatic	+	94	5.14	62.9	12.2
47	W	M	53	Normal	O	58	5.30	66.8	12.5
48	W	M	45	Bronchogenic carcinoma left upper lobe	O	104	7.52	102.9	13.6
49	W	M	63	Primary carcinoma left upper lobe	+	96	9.16	53.4	5.8
50	W	M	48	Asthma	+	71	6.66	33.1	4.96
51	W	M	46	Bronchiectasis	O	84	7.08	97.1	13.5

TABLE 1 (Continued)

				Diagnosis	Dyspnoea	VENTILATORY FUNCTION			
Age in	Sex	years				V C per cent	R M V Liters	M B C Liters	V R
52	W	M	60	Bullae	+	84	6 45	73 0	11 3
53	W	M	54	Silicosis	+	72	8 87	79 3	8 94
54	W	M	40	Asthma	O	82	6 15	98 5	16 0
55	W	M	59	Silicosis	+	76	7 06	68 0	9 6
56	W	M	49	Pulmonary tuberc	+	58	8 52	66 5	7 8
57	W	M	68	Bronchogenic carcinoma	+	67	7 49	42 7	5 7
58	W	M	57	Asthma	+	54	7 22	18 0	2 5
59	W	M	62	Silicosis	O	78	7 95	89 4	9 5
60	W	M	45	Chronic asthma	O	69	7 68	94 1	12 2
61	W	F	29	Bronchiectasis	+	62	7 00	44 1	6 3
62	W	F	42	Pulmonary tuberc	+	44	5 06	22 3	4 4
63	W	M	35	Pulmonary tuberc	O	56	7 20	77 2	10 7
64	W	M	54	Pulm fibrosis	O	90	6 21	92 0	14 8
65	W	M	54	Bronchiectasis	+	84	6 90	82 0	11 9
66	W	M	55	Chronic asthma	+	100	9 84	77 6	7 9
67	W	M	66	Bronchogenic carcinoma	+	62	6 00	64 0	10 6
68	W	M	41	Bronchogenic carcinoma	O	77	6 23	113 0	18 1
69	W	M	48	Chronic asthma	+	81	7 99	44 3	5 5
70	W	M	53	Cystic lung	O	56	6 95	50 7	7 3
71	W	M	33	Pulmonary tuberc	O	77	8 96	88 1	9 8
72	W	M	41	Bronchogenic carcinoma	O	38	6 96	78 1	11 2
73	W	M	59	Bronchiectasis 20 years	O	79	5 49	89 4	16 0
74	W	M	51	Pulmonary tuberc	+	51	9 51	63 1	6 9
75	W	M	49	Pulmonary tuberc	+	51	6 4	31 4	4 9
76	W	M	50	Bronchogenic carcinoma	O	71	10 3	70 9	6 9
77	W	F	56	Pulm carcinoma	+	80	5 55	34 4	6 2
78	W	M	63	Pulmonary tuberc	+	56	8 49	18 1	2 1
79	W	M	56	Pulm carcinoma	+	40	8 72	87 3	7 8
80	W	M	51	Pulmonary tuberc	+	57	9 7	60 3	6 2
81	W	M	37	Emphysema ?	+	95	8 42	69 8	8 3

Abbreviations V C = Vital capacity, R M V = Respiratory minute volume, M B C = Maximum breathing capacity, V R = Ventilatory reserve

- C) Third arm three-way stopcock to which the rebreathing bag (D) is attached
- E) Handle of stopcock for directing the flow of gas

### *Description (Figure 3)*

A rubber rebreathing bag (D) is fitted to the lower arm (C) of a three-way valve. A rubber mouthpiece (A) is attached to the inlet of the valve. The mouthpiece can be made to communicate with the outside air through opening (B) or with the rebreathing bag through opening (C) by turning the cock handle (E).

### *Directions for Operation of Test*

The rebreathing bag should be thoroughly "washed" with room air, and then emptied to eliminate gases remaining from the preceding test. Turn the cock so that the mouthpiece arm communicates with the open arm (B). Add 1000 cc of air to the bag (D) through the rubber inlet at the bottom. Clamp the inlet. The bag may be inflated with 1000 cc of air by utilizing a basal metabolism apparatus as a metering device or by the use of a calibrated pump or piston.

Rest the subject in a sitting position for a 30 minute period.

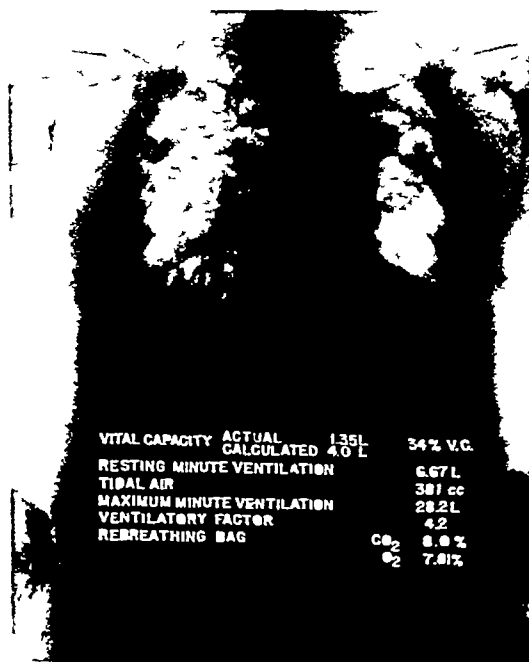


FIGURE 2

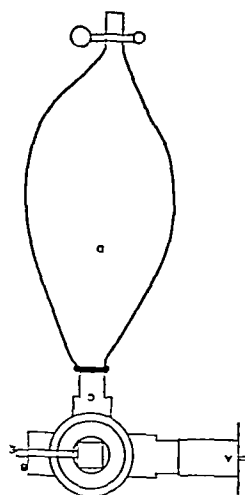


FIGURE 3

At the end of this period, place the mouthpiece in the subject's mouth and clamp his nose with a noseclip. The subject is then made to ascend and descend from an 8 inch step, thirty times in a period of one minute. Immediately after this exercise he is seated. At the end of a normal expiration the handle (E) of the cock is turned 90° to make the mouthpiece (A) communicate with the bag (D). The subject rebreathes from the bag for exactly 20 seconds. Then the cock is turned to the earlier position. The gas content of the bag is then analyzed for oxygen and carbon dioxide. The gases in the rebreathing bag are then withdrawn in the sampling tubes.

Analysis of the gases in the sampling tubes were then analyzed for oxygen by means of a Haldane-Boothby-Sandiford gas analyzer. There is a simplified (Ornstein<sup>8</sup>) equipment for estimating oxygen and carbon dioxide. The latter analyzer, while not as accurate as a Henderson-Haldane-Sandiford apparatus is far easier to operate. It has an accuracy of 0.1 per cent and its use can be mastered by a technician.

The following case reports demonstrate the value of a combined measurement of the ventilatory and diffusion tests.

*Case 1* A white male of 55 years of age who had been under clinical observation since December 23, 1926. In 1926 he consulted the author because of a severe hemoptysis. He had an atelectatic left lung due to a healed tuberculous disease. The left lung was reduced in size and the right lung occupied most of the thorax. His sputum examinations since 1926 were negative for tubercle bacilli. From 1926 to 1947 he had frequent attacks of hemoptysis which interfered with his routine life. In 1947 a decision was made to do a left pneumonectomy.

Because of the great hypertrophy of the right lung which had been present since 1926 a question arose as to the pulmonary function of the right lung (Figure 4). There is a common belief that once a lung hypertrophies it begins to become emphysematous and rapidly does so. A pulmonary function test was therefore done. The result was as follows:

			Calculated Normal V C
<i>Ventilatory function</i>			
Vital capacity	Actual	2.56 Liters	
	Calculated	4.45 Liters	58 per cent
Tidal air		745 c c	
Resting minute ventilation		5.49 Liters	
Maximum breathing capacity		74.5 Liters	
Ventilatory reserve		13.6	

#### *Pulmonary diffusion*

Rebreathing bag test,

O <sub>2</sub>	7.82 Vol per cent
CO <sub>2</sub>	8.05 Vol per cent

This function test was more interesting. Firstly, note that the vital capacity was misleading. The patient seemed to have a restricted ven-

tilation However, his ventilatory function was not reduced when you know that he had one lung functioning A pulmonary ventilation of 13.6 is not bad The astonishing fact was that a lung that had been hypertrophied for 21 years was able to diffuse oxygen normally

A pneumonectomy was done in April, 1947 The patient made an uneventful recovery and has been free of symptoms since He has been able to go back to his normal routine without any symptoms of dyspnoea

*Case 2* Case two is presented to confirm that a lung may be hypertrophied over a long period of time and not become emphysematous A white female of 44 years had an extensive pulmonary tuberculosis involving the left lung The tuberculous lung was collapsed with artificial pneumothorax in 1923 and the treatment abandoned after 2 years because of a complicating tuberculous empyema The tuberculous empyema was controlled by pleural aspirations and finally in 1926 the pleural cavity became obliterated The left lung became atelectatic and fibrotic and since 1926 the sputa have been negative for tubercle bacilli The tuberculous disease has been in a state of arrest since 1926 The right lung has hypertrophied and remained so throughout the past 21 years

The patient consulted the author last on March 26, 1947 concerning her pulmonary status She had no symptoms of dyspnoea and had no complaints The object of her visit was her concern about exercise in view of her old pulmonary tuberculosis She had begun to play golf and she was worried whether the exercise might reactivate her old tuberculosis She had no discomfort while golfing

Figure 5 is a reproduction of a roentgenogram taken on March 26, 1947 which revealed an atelectatic fibrotic pulmonary tuberculosis of the left lung The retraction of the left lung drew the heart and the mediastinum into the left thorax The right lung had hypertrophied and also occupied a part of the left thorax The roentgenogram was no different from the roentgenogram since 1926 The right lung had been hyper-

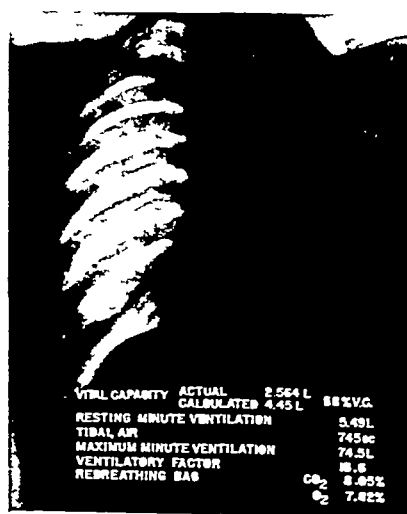


FIGURE 4

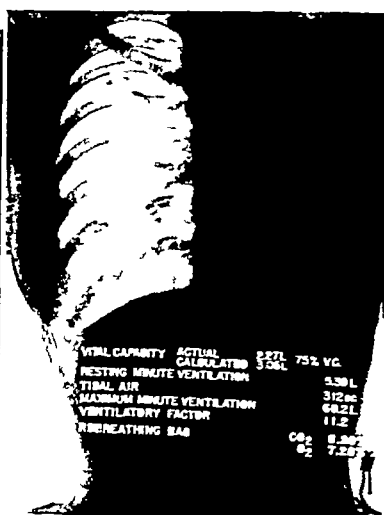


FIGURE 5



trophied for about 21 years A lung function test was done and revealed the following

<i>Ventilatory function</i>			Calculated Normal V C
Vital capacity	Actual	2 27 Liters	75 per cent
	Calculated	3 05 Liters	
Tidal air		312 c c	
Resting minute ventilation		5 39 Liters	
Maximum breathing capacity		60 2 Liters	
Ventilatory reserve		11 2	

*Pulmonary diffusion*

Rebreathing bag test,	
O <sub>2</sub>	7 20 Vol per cent
CO <sub>2</sub>	8 20 Vol per cent

The right lung had been hypertrophied for 22 years Again contrary to the prevalent impression that a lung that hypertrophies goes on to emphysema with loss of pulmonary function, this patient's hypertrophied lung has not done so The ability of the lung to ventilate and diffuse oxygen and carbon dioxide is still within the normal range

Case 3 A white male of 48 years had been occupied as a laborer He had asthma since he was twelve years of age At the age of twenty-one it had disappeared only to recur again in 1946 He stated he had a wheeze in his lungs at all times and he always had difficulty in breathing and fatigues easily on exertion Figure 6 is a reproduction of a roentgenogram that reveals two hypertrophied lungs with exaggerated bronchial markings in both lower lobes A pulmonary function test was done on February 1, 1947 and revealed the following

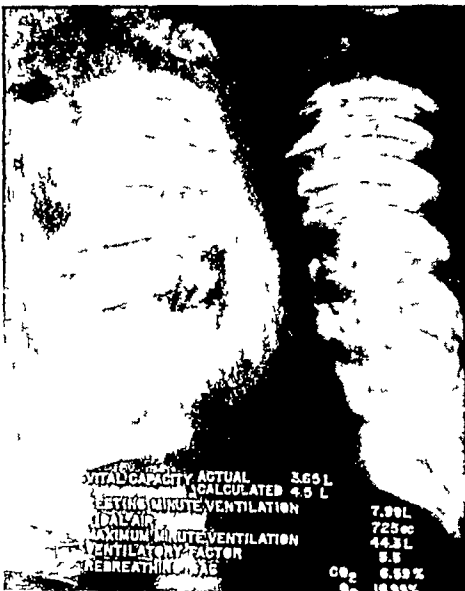


FIGURE 6

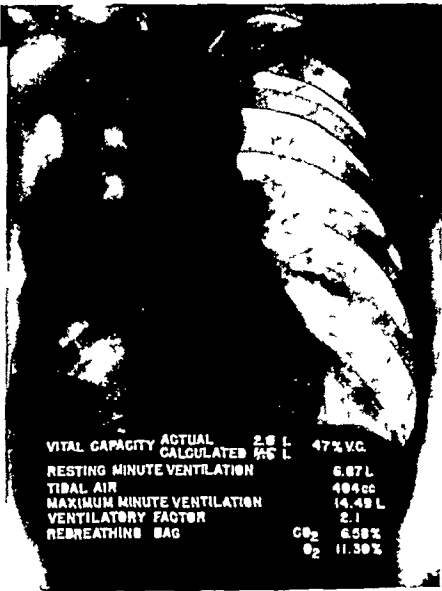


FIGURE 7

*Ventilatory function*

Vital capacity	Actual	3 65 Liters
	Calculated	4 5 Liters
Tidal air		725 c c
Resting minute ventilation		7 99 Liters
Maximum breathing capacity		44 3 Liters
Ventilatory reserve		5 5

*Pulmonary diffusion*

## Rebreathing bag test

O <sub>2</sub>	10 99 Vol per cent
CO <sub>2</sub>	6 59 Vol per cent

This case demonstrates there was both a ventilatory and diffusion disturbance

*Case 4* A white male of 54 years who had been ill with pulmonary tuberculosis since 1932 In 1934 he had a three stage thoracoplasty which controlled his pulmonary tuberculosis in his right lung Since then his tuberculosis has been in a state of arrest Since his operation he has been short of breath and fatigued on the least exertion

Figure 7 is a reproduction of a roentgenogram of his thorax The right lung had the usual shadows one sees following a thoracoplasty The left lung was hypertrophied A lung function test was done on September 4, 1946 and revealed the following

*Ventilatory function*

		Calculated Normal V C
Vital capacity	Actual	2 0 Liters
	Calculated	4 6 Liters
		47 per cent
Tidal air		494 c c
Resting minute ventilation		6 8 Liters
Maximum breathing capacity		14 49 Liters
Ventilatory reserve		2 1

*Pulmonary diffusion*

## Rebreathing bag test,

O <sub>2</sub>	11 30 Vol per cent
CO <sub>2</sub>	6 58 Vol per cent

This patient had a very low ventilatory reserve, 2 1 times his resting minute ventilation He also has a marked disturbance in his pulmonary diffusion as evidenced by the high volumes per cent of oxygen in his rebreathing bag (11 30 Vol per cent)

## SUMMARY

A method is given of measuring both the ventilatory and the diffusion functions of the lungs

## RESUMEN

Se presenta un método para medir tanto la función ventiladora como la función difusora de los pulmones

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## D i s c u s s i o n

BENJAMIN P POTTER, MD, FCCP

Jersey City, New Jersey

The method described by Dr Ornstein has merit even if it does nothing more than to indicate the alveolar concentration of gases. The fact that cardiorespiratory physiology is still in a rather flexible state should make welcome any new method which may clarify the subject.

As a clinician, I have been unfavorably impressed with the confusing terminology and the varied interpretations assigned to test for pulmonary function, to say nothing of the numerous tests used and the new ones which continually are advanced for evaluation of the same problem. Before useful application of recorded studies can be made, acceptance of universal terms and coordination of the various tests should be arranged. In this respect our College can offer a much needed contribution.

Everyone has been impressed with the importance of knowing the patient's respiratory reserve prior to surgical collapse for pulmonary tuberculosis and, in more recent years, prior to excision therapy for this disease as well as for non-tuberculous conditions of the lungs. While the crude tests mentioned by Dr Ornstein are often sufficient, retrospect observations suggest that many postoperative deaths previously ascribed to cardiac failure were,

likely, due to respiratory or cardiorespiratory insufficiency as judged from the more accurate data obtainable by present day studies of respiratory capacity

At the same time it should be recognized that the tests do not replace careful and mature clinical judgment of the patient's ability to withstand surgery, made over a period of time as contrasted with the evaluation arrived at after one or two sittings required for the studies of respiratory function. In fact, unless one remembers that no test is free of the "psychogenic factor"—or what is more often referred to as the need for the patient's cooperation—and that breathing is done under some stress connected with the artificiality of the tests, one is likely to attach too much importance to the final results. This point can be compared with the hasty unfavorable conclusion drawn, at times, by both surgeons and internists after reviewing a series of roentgenograms, clinical data, and a view of the patient at a medical surgical conference. The contrary opinion of an experienced physician who has attended the patient for a longer period of time is often of greater value.

In cases in which the respiratory reserve is borderline or poor, surgery should not be denied the patient if the attending physician's observations do not corroborate those of the physiologist. I now have a fair number of instances in which surgery was denied the patient because of physiologic studies indicating inadequate respiratory reserve, but was subsequently performed on the insistence of the clinician and resulted in effective collapse and adequate residual respiratory function.

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ALVAN L. BARACH, M.D., F.C.C.P.  
New York New York

One of the things we want to know before operating on a patient is how short of breath he will be after operation, and it may well be that the test Dr. Ornstein has devised will be of considerable help. To understand the significance of the test, it would be desirable to correlate it with other observations, such as the breath-holding time. That is an extremely simple test and is of value.

The influence of anoxia on dyspnea and pulmonary ventilation, both in the normal person and the one with chronic respiratory disease is important. At an altitude of 10,000 feet there is increased pulmonary ventilation, measured carefully by Engel and Ferris, increasing every 2,000 feet. In patients with respiratory disease

such as pulmonary emphysema, it is often of great help to determine their respiratory function, to test the volume of breathing, to determine the difference between breathing air and breathing oxygen. A man breathing 12 liters a minute may, within five minutes of breathing 100 per cent oxygen, reduce his ventilation to 8 to 10 liters per minute. This gives a considerable clue to that particular person's dependence upon oxygen.

Even though the arterial oxygen saturation may be at that time 95 per cent, it is a misunderstanding to say that lack of oxygen or anoxia or hypoxia is not involved, simply because his oxygen saturation is normal or nearly so. It is evident that these people are making sufficiently burdensome efforts to ventilate their lungs to give them dyspnea and acute distress, and this increased ventilation happens at times to result in saturation that is almost normal. However, in almost 95 per cent of patients with hypertrophic pulmonary emphysema, there is marked reduction in pulmonary ventilation after four days inhalation of a 50 per cent oxygen atmosphere. We may think of dyspnea in chronic respiratory disease as a combined effect of (1) increased ventilation, (2) the capacity of the individual to provide this increased ventilation without distress and (3) the capacity of the individual to maintain a normal hemo-respiratory exchange.

It will be of considerable interest and profit to us to watch the further observations of the diffusion method of Dr. Ornstein. I should like to ask him whether he has been able to separate diffusion through the lung parenchyma, through the pulmonary capillaries, from diffusion within the lung itself. We know that irregular ventilation of the alveoli takes place in pulmonary emphysema. There are sometimes large dead spaces in which failure to absorb oxygen does not come from impairment of the pulmonary capillaries, but from waste spaces where air is present, not exposed to the capillaries at all. There are of course many other factors that are important, such as the difference in ventilation before and after inhalation of bronchodilators, the degree with which many patients with chronic pulmonary disease fail to use the diaphragm although they are partly able to do so. In periods of distress, naturally the costal and neck muscle respiration predominates. The pulmonary ventilation may be high. But many of these people can be taught to use the diaphragm, which they have forgotten to use because of the panic brought on by extreme dyspnea. With diaphragmatic breathing the maximal pulmonary ventilation may increase.

I am now making a plea to correlate the tests we have already learned with the new tests so interestingly presented to us this morning.

EDWIN R. LEVINE, M.D., F.C.C.P.  
Chicago, Illinois

It is notable that physiology is beginning to come out of the laboratory into clinical medicine. Work which can be done only by highly trained research individuals, has clinical value only by indirection. When a physiologic technic can be made available to any hospital, to any clinical group, then that technic begins to have clinical importance. The work presented today shows how we can think in terms of doing physiologic testing even as we do blood testing and x-ray.

We should remember that decompensation and disability of patients does not always come from damage to the lung, or does the lack of such disability always indicate lung function. We are aware of the fact that emphysematous patients do not have slowly developing disability, but go along for some time and then suddenly, by some mechanism or some intercurrent infection, show marked change and disability, and the disability frequently continues and is progressive. It sometimes impresses me like stepping off the roof of a building, one day a man seems able to do his work, and two or three days later he is completely disabled. It appears to be a breakdown in the compensatory mechanism rather than marked change in the lung function itself.

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GEORGE G. ORNSTEIN, M.D., F.C.C.P.  
New York, New York

In reply to Dr. Barach I would like to say that for the past four years at Sea View Hospital and the Metropolitan Hospital every patient who had a problem of dyspnea has gone through this test. We are now doing these tests at Halloran Hospital and at my office, and thus are accumulating hundreds of cases. It is not just a question of a small group. We would not consider thoracic surgery unless the patient had a good diffusion test. We are willing to go along with lower ventilation but not with poor diffusion. Any doctor associated with a large institution where much thoracic surgery was done would know of a large number of physiologic cripples who had recovered from their disease but who, after surgery, had never been able to walk far from their chairs. Whether or not pulmonary surgery should be done in such cases is questionable.

One interesting thing we have learned, particularly in pneumonectomies, of which we have done many at Sea View, is that a thoracoplasty following pneumonectomy cuts down the ventilation markedly. Inasmuch as we believe that the remaining lung

may hypertrophy and not become emphysematous, it is wiser to allow that lung to take up the whole thorax and it may ventilate and diffuse better than by restricting the thorax with thoracoplasty after pneumonectomy. This year we are attempting to use the diffusion test in bronchspirometry. We started the work at the Metropolitan Hospital, where we are trying to create an oxygen debt with an arm weight exercise. In bronchspirometry the other day we had a patient with a good diffusion test. We knew by our fluoroscopic studies that one lung was doing most of the functioning, and we had the usual picture of one lung ventilating poorly and the other doing most of the ventilation. The amazing thing was that in both lungs, in spite of the variation in ventilation, the oxygen equivalent was about the same, about three liters. In bronchspirometry, under resting conditions, unless an oxygen debt is produced, the lung that ventilated poorly but apparently diffused well, might have shown its permeability defect could we have produced an oxygen debt.

Dr Barach brought out an interesting question of irregular ventilation and irregular diffusion in parts of the lung which do not ventilate. The above surprised us more than anything else. We took a group of normal individuals who had normal diffusion tests and cut down their ventilation by putting them in canvas jackets, thus reducing the ventilation. We had one man strapped down to 25 per cent of his normal vital capacity, yet the diffusion tests were exactly alike whether the ventilation was good or poor. So the two systems of ventilation and diffusion have no relationship. Usually where there is good ventilation there is also good diffusion, but we have had cases where ventilation was good and diffusion poor. On the other hand no matter how low the ventilation there may be good diffusion. Whether the small area of lung tissue being ventilated is sufficient under effort to supply the entire blood stream with oxygen is hard to say. Unfortunately, when a patient has a great deal of anoxia no physiologic test is needed, you can see it with your eyes. But as a rule people with impaired diffusion and ventilation are comfortable when at rest, and if diffusion tests are done at that time and compared to normal, without developing an oxygen debt, they will be found pretty close to normal. One cannot know the capability of the lung to diffuse oxygen unless an oxygen debt is produced.

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GEORGE E WRIGHT, M D  
Saranac Lake, New York

I think it might clarify things somewhat if Dr Ornstein would tell us what he means by ventilation. There is as yet no un-

animity in the way we use these terms. When I speak of ventilation I mean the distribution of gases in the lung. For example, whether a room is well ventilated depends on the amount of fresh air that comes into the room and, equally important, how it is distributed. If I understand Dr. Ornstein correctly, he means simply the amount of air moved into and out of the lung. It is not surprising that Dr. Ornstein finds no change in the diffusion test when he straps the chest. After all, he has not changed the efficacy with which the lung can be ventilated by simply strapping the chest, all he does is reduce the maximum ability of the respiratory apparatus to move air in and out of the lung. So long as the subject can still move the required one liter back and forth, there should be no evidence of abnormality in the test.

I am delighted that Dr. Ornstein has simply ignored certain *a priori* objections to this method and proceeded with these studies, because information has been brought out that is of use. I think, however, that Dr. Barach's comment regarding the necessity of correlating a test with other things is apropos, particularly with regard to Dr. Ornstein's work. I am loath to accept this as a method for testing diffusion across the membranes until he can show that it correlates well with a measured abnormal oxygen and  $\text{CO}_2$  tension in the blood during exercise. It would be of interest also if he would tell us how many cases he predicted would do poorly and which he subsequently found did so when operated upon.

I should like to know how many cases were operated upon that Dr. Ornstein said should not be operated upon, and of these how many turned out well and how many turned out poorly.

In our experience we have not been particularly keen to have operations on emphysematous patients. But we have found to our pleasant surprise—at least in 10 or 12 cases—that the surgeon can operate successfully on persons with severe emphysema if the operation is done in small stages, at times they have done one rib at a time. The emphysematous patient does not tolerate well a soft chest wall in the immediate postoperative period, but if the area is kept small many patients with emphysema can be carried successfully through a surgical procedure.

Dr. Barach's comment on hypoxia points out the difficulty of making oneself clear. I certainly do not deny that hypoxia will drive the respiratory center in abnormal fashion, -I know it will. The point I wish to make is that it does not always do it. The variations in sensitivity of the chemo receptors to oxygen are well known. There is a difference between the reactions of a group of normal persons suddenly exposed to low oxygen tensions, and a group of patients who have lived with hypoxia for one, three



or four years. Some patients are able to go around with arterial oxygen tensions as low as 60 mm of mercury, and hemoglobin saturation as low as 85 per cent, and when measured for ventilation response during exercise, they show no abnormality. I think one is forced to conclude from such studies that hypoxia does not always produce hyperventilation.

One other point should be considered, it is difficult to divorce the physiology of the circulatory system from that of the respiratory system. And the effects of poor blood supply to the tissues cannot be ignored in making studies of pulmonary function. Until better ways are devised for studying the circulatory and the respiratory system, this confusion will exist and many curious findings will occur.

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GEORGE G ORNSTEIN, M D , F C C P  
New York, New York

With the presentation of any new work, other investigators usually are skeptical only because they are not familiar with the new work and are hesitant to accept it. Is it not likely that when a new test for pulmonary function is reported in the literature, other investigators will repeat the work and either prove or disprove it? My group has presented these studies in the literature over the past few years and up to this time there has been no disconfirmation of our efforts. On the other hand, the tests have been applied clinically in all cases to have thoracic surgery at Sea View and Metropolitan Hospitals, and have been of great assistance in the selection of patients. Dr Wright stated that we should do the oxygen volume per cent of the blood in conjunction with our rebreathing bag test before he could accept our work. However, up to the present time no one has reported any work disproving our claims for the value of the test.

We are now doing the gas volume percentage of the blood in conjunction with the rebreathing bag tests. This was not possible until we had the technical help that can accurately use a tenometer, with which few technicians are familiar. Our results on this will be reported in the near future. It was necessary to work out a new exercise test, the step exercise test could not be used as our samples of blood are taken from the femoral artery. With the development of a new exercise test in the recumbant position so that we could use an indwelling catheter in the femoral artery, we have had to establish new controls. The basic work has been completed and we will now be able to report the oxygen volume per cent in the rebreathing bag and in the femoral artery occurring at the same moment.

Up to the present time we have done many hundreds of function tests and the patients, following operation, have shown that the tests have prophesized that they would not be pulmonary cripples so far as pulmonary function is concerned

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GEORGE E WRIGHT, MD  
Saranac Lake New York

In general I do not like to discuss a method that I have not used personally In our laboratory we try to study carefully all aspects of any method we devise before we make any statements concerning it It is unusual for an investigator to publish a method without determining at least the elementary and fundamental controversial aspects of the procedure It is indeed a new trend to expect others to do it for him

There is no question about Dr Ornstein's factual findings, namely, that oxygen tension did not drop as low in some of these cases during rebreathing as it does in others The interpretation is the point, I think, upon which we differ He has not, for example, shown us any evidence wherein he has controlled the size of the lung at the time the man is turned into the rebreathing bag From a mathematical standpoint one can calculate that in a man with a large mid capacity the result that should be obtained with his method is exactly what he actually does get, and it has absolutely nothing to do with the passage of oxygen across the alveolar membrane In other words, he starts out, in people with emphysema, with a large total volume of air to breathe in 20 seconds than he does in the normal man, therefore, given the same amount of oxygen consumed per minute, he must end up with a higher oxygen tension in the rebreathing bag of the emphysematous patient I think the method should be considered as one for study of lung volume rather than for diffusion of oxygen or  $\text{CO}_2$  across membrane The method may have some use when it is properly correlated with other factual data, until that is done, however, it cannot be accepted without some reservation

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ALVAN L BARACH, MD FCCP  
New York New York

I think one observation might clarify what I think is a somewhat confused point in this discussion When we speak of ventilation of the lung, are we speaking of just the amount of air that goes in and out of the lung, or are we speaking also of alveolar ventilation? Just compressing the chest does not duplicate what

happens in the patient with pulmonary fibrosis and pulmonary emphysema. The lung volume and ventilation of the patient with pulmonary emphysema may be markedly changed by manually elevating the diaphragm. Pushing up the diaphragm 10 times during expiration, particularly after inhalation of a bronchodilator substance, increases the vital capacity 1,000 cc a minute and a half afterward. The patient's sensation of dyspnea may have disappeared. He had been breathing a high pulmonary ventilation, he had had a large volume of air (high residual air) with which to dilute any gas, but his alveolar ventilation was poor.

I think it would be interesting to Dr. Ornstein and to Dr. Wright, and to myself, to do this test after manual elevation of the diaphragm, i.e., get the per cent  $\text{CO}_2$  and oxygen in the bag when a man has an overfilled lung, and then squeeze out 800 or 1,000 cc of air and see what the chest shows afterward.

I am sure that you cannot in this test separate the effects of diffusion of air within the lung alveoli, particularly in the damaged lung, from diffusion across the capillaries, large areas of emphysematous lung are irregularly inflated, sometimes five minutes may pass before some area opens up. In other words, in the test there are two factors, one is diffusion of air within the lung itself, particularly in cases of emphysema, and the second factor is the diffusion of gases across the pulmonary capillaries. These two separate functions are included in the test as I see it, total pulmonary ventilation may also be high with poor alveolar ventilation.

## Comments on Bacterial Resistance to Streptomycin\*

ARNOLD SHAMASKIN M.D., F.C.C.P., F.A.C.P.\*\*

Hines Illinois

Shortly after streptomycin was introduced in the treatment of tuberculosis, two major obstacles to its value as a therapeutic agent became apparent. These were, vestibular damage and development of bacterial resistance. With the reduction in the daily dosage from 2 gm and higher, to 1 gm and later to 0.5 gm, serious vestibular damage has been eliminated. However, development of bacterial resistance, which is apparently due to duration of treatment rather than to dosage, remains for the present the most serious threat to successful streptomycin therapy in tuberculosis. With the appearance of resistant forms of tubercle bacilli, streptomycin ceases to be an effective therapeutic agent not only for the individual patient but also for those to whom he may transmit the disease.

Youmans and Williston<sup>1</sup> found that when a group of mice were injected intravenously with 0.1 mg of a culture of tubercle bacilli isolated from a patient with pulmonary tuberculosis, streptomycin had a marked suppressive effect on the infection produced in the animals. On the other hand when a group of mice were injected in the same manner with a culture of tubercle bacilli from the same patient after he was treated with streptomycin, the infection resulting from it was uninfluenced by the drug.

Bogen<sup>2</sup> related the case of a nurse who contracted tuberculosis while working with streptomycin treated patients. Tubercle bacilli recovered from this case were resistant to 1000 micrograms per cc on original isolation.

It is obvious why the study of bacterial resistance to streptomycin and specifically the search for measures to prevent it are occupying a very prominent place in this field of investigation.

The theory behind the development of bacterial resistance to streptomycin is based on the knowledge that probably every case of tuberculosis harbors different varieties of tubercle bacilli. By

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\*From the Tuberculosis Service, Veterans Administration Hospital, Hines Illinois. Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or the conclusions drawn by the author.

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far the vast majority of organisms are sensitive to streptomycin but an occasional form is by nature resistant to the drug. It is undoubtedly for this reason that a favorable initial response to streptomycin is shown by almost every patient who has active and progressive tuberculosis and is not moribund and that, if treated long enough, probably every case acquires resistance to streptomycin sooner or later.

It may be reasoned that under streptomycin therapy all the sensitive organisms are inhibited and are either prevented from multiplying altogether or their rate of reproduction is greatly reduced. Thus the army of invaders becomes reduced at a fairly rapid rate when exposed to the drug. While the vast number of sensitive organisms are thus held in check by streptomycin, the natural defensive forces of the body come into play, assume dominance, and begin to recover lost ground. It is apparent then that the time during which effective use of streptomycin can be made is limited to the minimum time required by the streptomycin resistant organisms to increase in sufficient numbers to become a potent force against which streptomycin is a useless weapon.

No relationship has been found to exist between the degree of sensitivity of tubercle bacilli to streptomycin and the degree of their virulence. Either variety may be of high or low virulence. Both varieties work hand in hand and each contributes its share to the clinical picture in proportion to its numerical strength as well as to degree of virulence.

The rationale of the various methods proposed for combating the development of resistance is predicated upon the speed with which the enemy must be overcome. In other words this must be a "blitz" campaign which would enable the patient to overcome the disease in the shortest possible time before the streptomycin resistant organisms can multiply sufficiently to become effective and to take over the situation.

Since resistant strains of tubercle bacilli usually begin to make their appearance before the end of the second month of treatment, shorter periods of treatment than 60 days have been advocated and are being tried. Simultaneously other drugs such as promizole and para-aminosalicylic acid are being investigated for the value they may have as auxiliary weapons against the tubercle bacilli, with the hope that they may act on the resistant forms when administered in conjunction with streptomycin.

It is also hoped that further research may bring forth other antibiotics which could be used for the treatment of tuberculous patients whose organisms have become resistant to streptomycin.

Meanwhile a plea is made against the indiscriminate use of streptomycin as a so-called "additional boost" for the treatment

of comparatively mild tuberculous lesions which are very likely to regress or have already shown evidences of satisfactory regression both clinically and roentgenologically under adequate conventional therapy Abuse of the drug may deprive the patient of its benefits should he ever need it more urgently It also helps to perpetuate in the community a form of tuberculosis on which streptomycin has no effect While administering to the individual patient, the public health interests must not be lost sight of

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# Extrapleural Pneumothorax\*

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*Introduction* In the past ten years or so numerous conflicting reports have appeared in the medical literature concerning the efficacy and value of extrapleural pneumothorax in pulmonary tuberculosis. After Graf and Schmidt<sup>1</sup> in 1936 and 1937 published their very favorable results obtained with this form of temporary collapse therapy, there was an almost immediate world-wide manifestation of renewed interest in the procedure originally described and developed by Tuffier<sup>2</sup> many years previously. The initial wave of favorable reports from the pens of enthusiastic advocates, however, was soon followed by equally numerous and authentic unfavorable reports by the critics of this procedure. As a result of these conflicting opinions, extrapleural pneumothorax, today, occupies a very questionable and controversial position in the phthisiologist's therapeutic armamentarium.

This study was undertaken in order to present a statistical analysis of our own experiences and results with this form of collapse therapy in a large series of cases. We trust that this evaluation will help to classify the procedure correctly and not add to the existing confusion. All of the cases used in this report are from Jefferson County Tuberculosis Sanatorium and all the surgery was performed by Dr. L. O. Davenport.

*Materials* (Table I) From October 1939 through December 1946, a total of 141 patients had extrapleural procedures performed at the Jefferson County Tuberculosis Sanatorium. In selecting cases for study only 97 were considered satisfactory for evaluation. The remaining 44 patients are not included in this study as the available data in these cases was considered insufficient or unsatisfactory for meaningful evaluation. Bilateral extrapleural pneumothorax was established in 4 of the studied cases (figure 2) while 3 other patients in this group had two-stage extrapleural pneumothoraces (figure 7). One hundred and four extrapleural procedures are therefore available for this study. In 7 of the cases studied the extrapleural pneumothorax was combined with a

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\*From the Jefferson County Tuberculosis Sanatorium, Birmingham, Alabama. Presented at the Thirteenth Annual Meeting of the American College of Chest Physicians, June 5, 1947 at Atlantic City, New Jersey.

preexisting intrapleural pneumothorax (figure 6) Twenty-four of the extrapleural spaces were maintained with oil (figures 1, 2)

*Operative and Immediate Post-operative Technique* The simple pre-operative preparations include a saline enema, a barbiturate and a mild hypnotic prior to surgery The patient is then placed

TABLE I

Cases Followed	97
Cases not Followed	44
Total Number of Cases	141
Total cases available for study	97
Bilateral extrapleural pneumothorax	4
Two-stage extrapleural pneumothorax	3
Total extrapleural procedures followed	104
Total extrapleural procedures not followed	44
Total	148

## MISCELLANEOUS

Combined intra and extrapleural pneumothorax (one accidentally)	7
Collapse maintained with oil	24

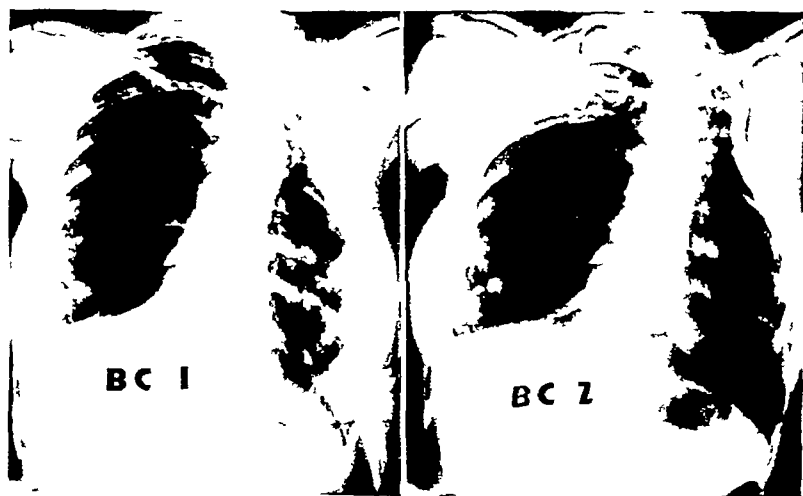


FIGURE 1 B C a 26-year-old white female Had thoracoplasty on left side following which a large thin-walled cavity developed on the right side (1) Could not establish intrapleural pneumothorax on right side and thoracoplasty was not possible because of patient's generally poor condition Extrapleural pneumothorax was established on 2-12-42 Converted to oleothorax in 1944 when patient could no longer manage to arrange for air refills Sixty-five months later (2) the disease was completely arrested and patient was enjoying a practically normal existence



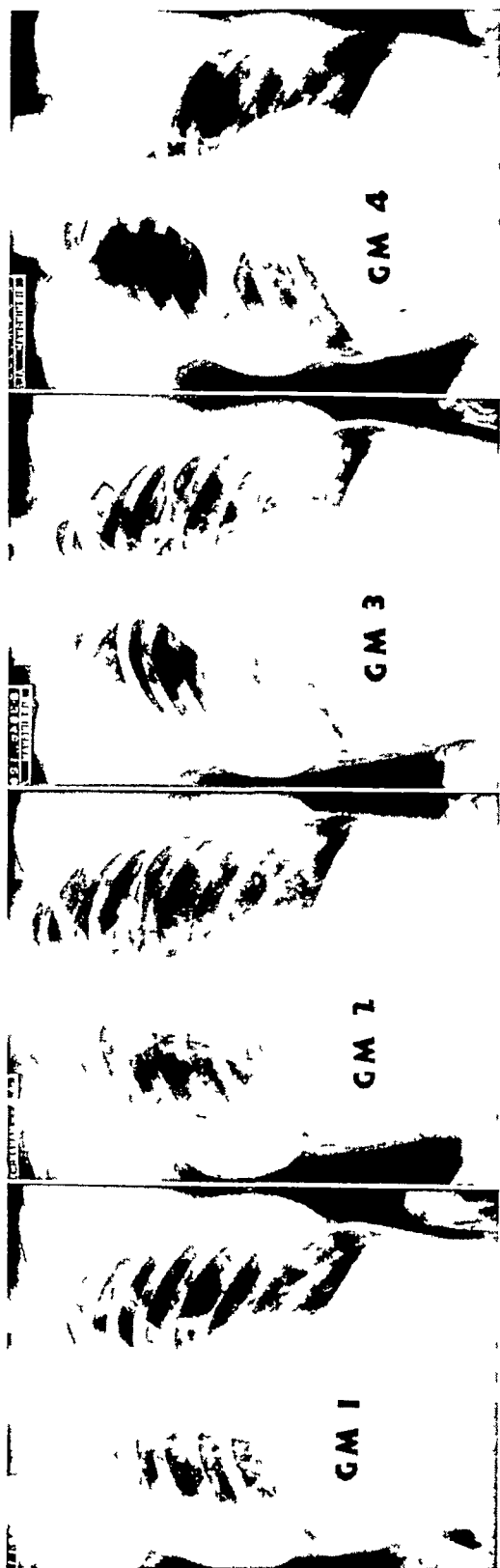


FIGURE 2 G M, a 27-year-old white female Intrapleural pneumothorax had failed on both sides (1) Patient was very uncooperative Left extrapleural pneumothorax established on 3-14-46 (2), followed by right extrapleural pneumothorax (3) Left converted to oleothorax when patient left sanatorium against advice of physician Sixteen months later (4) patient is making good progress Since leaving the sanatorium has managed to contract syphilis in addition to pulmonary tuberculosis

on the operating table in a lateral position, the same as is normally used for thoracoplasty. All cases in this series were performed under local anesthesia (novocaine 1 per cent). Since 50 per cent or more of the lung is collapsed in a few minutes time, there is always some secretion expressed from the collapsing lung. With novocaine anesthesia patients are able to cough and expectorate several times during the operation which normally lasts 30 to 40 minutes. After infiltration of the skin, subcutaneous tissue and regional muscles is accomplished with the anesthetic agent, a linear incision 10 to 12 centimeters long is made midway between the spine and the mesial border of the scapula, and extended down to the ribs. The intercostal nerves supplying the surgical field are blocked with a 1 per cent novocaine solution. The posterior serratus muscle is then freed from its attachment to the fourth and fifth ribs and retracted. This muscle is often of great value in effecting an air-tight closure. Seven to eight centimeters of the fourth rib is resected periosteally. Through the rib bed the extrapleural fascia is separated and the extrapleural space developed. The separation is extended as far as possible with the finger. Then the lung is depressed with an Overholt lighted-retractor and the separation continued with hard gauze sponges on long curved forceps. During this part of the operation great diligence must be exercised to avoid tearing the pleura.

We have found that the collapse obtained will not be adequate or satisfactory unless the extreme apex is separated from the dome of the pleural cavity. The dissection on the mediastinal surface is carried to the arch of the aorta on the left and to a comparable level on the right. On the posterior, lateral, and anterior pulmonary surfaces the separation is extended downward to well below the diseased area. Before closing, the extrapleural pocket is inspected carefully for bleeding points. These can usually be controlled by hot saline packs. Occasionally, a persistent bleeding vessel requires the application of one of the newer hemostatic agents such as thromboplastin. The periosteum and intercostal muscles are approximated by a continuous suture of chromic O catgut, and the posterior serratus muscle is drawn over and fixed to reinforce the suture line. Finally, the trapezius and rhomboid muscles and fascia are closed by a continuous suture of catgut, and the skin is repaired with silk.

At the end of the operation a pneumothorax needle is inserted into the newly established extrapleural space. Usually, a neutral reading is recorded and air is injected until a manometric reading of approximately +6 cm of water is obtained. About 8 hours later, a second refill is administered until the extrapleural pressure is raised to +8 cm of water. Twenty-four hours later the

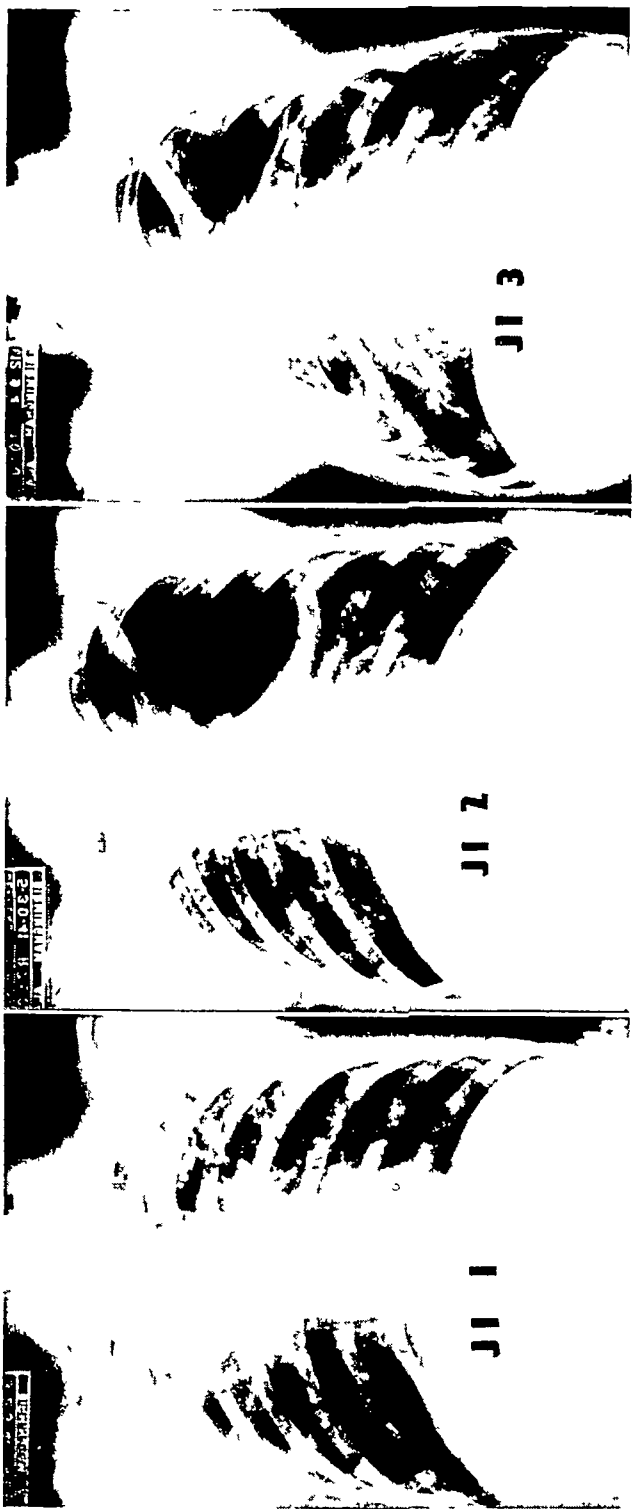


FIGURE 3 J I a 30-year-old white male Condition hopeless (1) Left extrapleural pneumothorax established 1-9-41 with good results (2) Followed by thoracoplasty on right Disease arrested and patient doing very well 78 months later (3)

pressure is increased to +12 cm of water. Following this refill, air is administered every 3 to 4 days during the immediate post-operative period.

A serosanguineous exudate always develops in the extrapleural space but no attempt is made to aspirate this fluid until the sixth or seventh postoperative day. At this time, the patient is seated in an erect position and aspiration is performed with a 15 or 16 gauge needle, 2½ to 3 inches long, through the second interspace. To avoid future complications, the extrapleural space should hereafter be kept as dry as possible with frequent aspirations until no fluid reforms. If the fluid continues to remain very sanguineous, the extrapleural space is washed with isotonic saline solution when necessary.

In order to maintain the maximum and necessary amount of therapeutic collapse, it is necessary to maintain a positive pressure in the extrapleural space at all times. If the pressure accidentally becomes neutral or negative between refills, the space will gradually be obliterated. At the end of two weeks of gradually increasing positive pressure in the extrapleural space, patients usually will tolerate a closing pressure of +24 to +30 cm of water. The degree of positive pressure obtained in the extrapleural space usually determines the frequency of refills.

*Distribution of Cases Followed by Color, Sex and Age* (Table II)  
Of the 97 patients 81 were white and only 16 were negroes. Although the white inhabitants of the sanatorium outnumbered the negroes, the latter discrepancy cannot be explained on this basis. Rather, it is felt that the condition of the negro patients who were successful in gaining admission to the sanatorium was generally so hopeless that not many were actually candidates by any standards for this type of surgery. Sixty-seven (69 per cent) were female and 30 (31 per cent) were males. This difference is

TABLE II

*Distribution of Cases Followed by Color, Sex and Age*

Age Groups	WHITE (81)		COLORED (16)		TOTAL (97)	
	Male 29.9 Pct	Female 70.1 Pct	Male 37.5 Pct	Female 62.5 Pct	Male 31 Pct	Female 69 Pct
10-19	2	4	0	1	2	5
20-29	6	27	3	6	9	33
30-39	13	17	1	2	14	19
40-49	2	7	1	0	3	7
50-59	1	2	1	1	2	3
Total	24	57	6	10	30	67

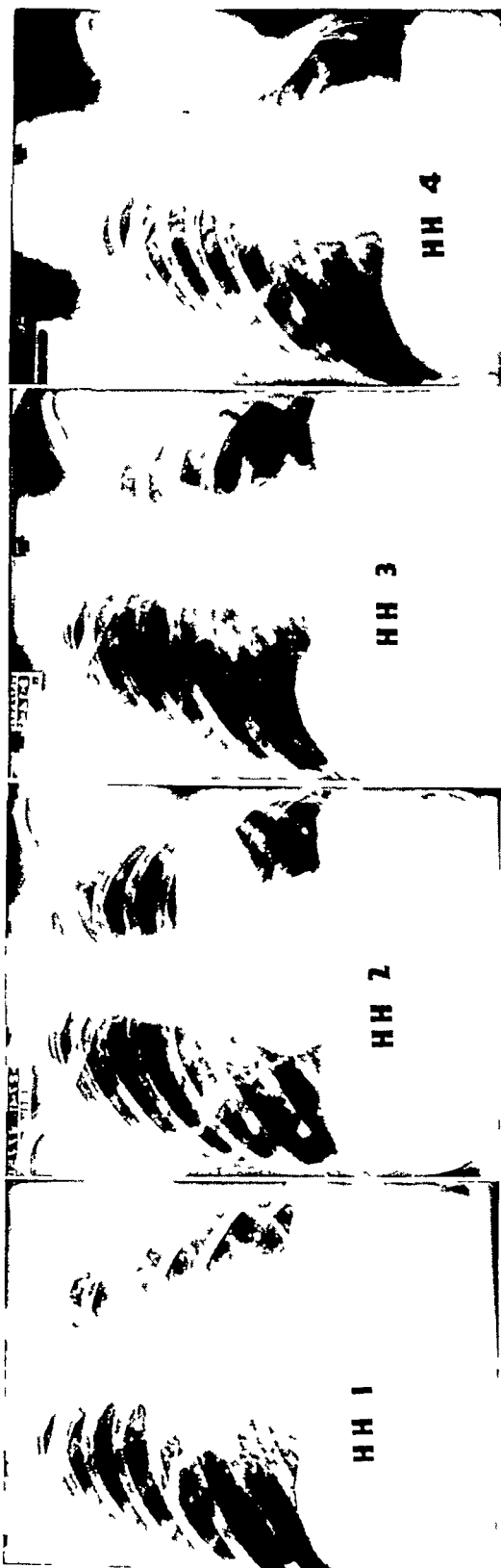


FIGURE 4 H H a 31-year-old white male In hopeless condition Bilateral far advanced exudative-cavernous disease Right intrapleural pneumothorax in progress Left failed (1) Extrapleural pneumothorax established 9-4-41 (2) Right side reexpanded following improvement Extrapleural pneumothorax unsatisfactory but halted progress of disease in left lung (3) Thoracoplasty performed on left side Sixty-nine months later disease arrested and patient engaging in useful activity (4)

attributed to two main reasons. For one thing, cosmetic considerations prompted females to accept this procedure in preference to a deforming operation such as a thoracoplasty, even when the latter was actually the procedure of choice. In addition, there is some discrepancy in the sanatorium population ratio which favors the females. The youngest patient in this series was a 14 year old colored female while the oldest was a 58 year old male. The former died within 8 months after surgery, and in the latter case the operation failed because a dense pachypleuritis made the procedure impossible. More than half of the patients were from 20 to 39 years of age. In view of the usual age distribution in tuberculosis sanatoria and for tuberculosis in general, the latter observation has no particular significance.

*Indications for Extrapleural Procedure in Group Followed* (Table III). Only after a fair trial of intrapleural pneumothorax and bed rest had failed to control the disease was any patient in this group considered as a possible candidate for extrapleural pneumothorax. In addition, many had had unsuccessful phrenic nerve operations. Forty-three (41.3 per cent) of the procedures were performed in hopeless cases (figures 1, 3, 4 and 7). The nature of the disease or the condition of the patient in these instances was such that thoracoplasty was beyond reasonable consideration. Twenty-nine (27.9 per cent) procedures were performed as the surgeon's choice (figure 9). The bulk of the cases in this classification were selected early in the series when the numerous enthusiastic and favorable reports actually led the surgeon as well as the patient to believe that the procedure was preferable to thoracoplasty (figure 2). In some of these instances extrapleural pneumothorax was established as a preparatory measure for future thoracoplasty (figures 3 and 4) on the ipsilateral or contralateral side. In recent years this situation has more than reversed itself and only very few are performed in preference to thoracoplasty while many more are established in preparation

TABLE III  
*Indications for Extrapleural Procedure in Group Followed*

	Total	Per Cent
1 Hopeless	43	41.3
2 Surgeon's Choice	29	27.9
3 Patient's Choice	32	30.8
a) Refused thoracoplasty	17	
b) Cosmetic reasons	15	
Total	104	100.0

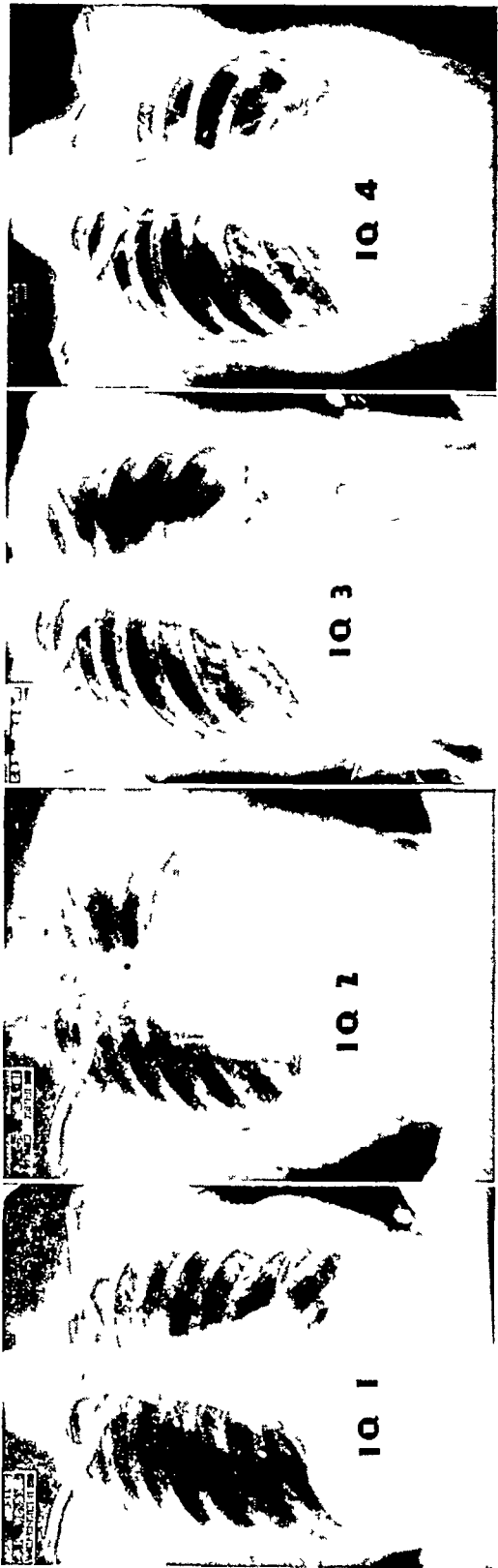


FIGURE 5 I Q, a 28-year-old white female, left and right intrapleural pneumothorax and left phrenic nerve crush failed to control disease. Refused thoracoplasty because of fear and cosmetic considerations (1) Extrapleural pneumothorax established 10-2-39 (2) Notice immediate postoperative fluid and emphysema in subcutaneous tissues of neck. Four weeks later (3) fluid almost completely reabsorbed and a successful extrapleural space achieved. Ninety-two months later the lung is reexpanded (4) disease is arrested and patient is in excellent health

for future thoracoplasty Extrapleural pneumothorax is an excellent temporizing and preparatory measure for a possible future thoracoplasty Preparatory extrapleural pneumothorax by temporary control of the pulmonary disease and fixation of the mediastinum in many cases (figure 4) insures the maximum therapeutic benefits which may be expected from an eventual thoracoplasty Many patients who otherwise would be left at the mercy of a progressive and fulminating disease can be benefited by utilizing extrapleural pneumothorax in this fashion The remaining 32 (30.8 per cent) of the procedures were performed at the patient's choice (figure 5) Some had read glowing newspaper accounts reporting the success of extrapleural pneumothorax as a collapse measure, and others were influenced by the very fear of surgery and prolonged convalescence involved in accomplishing a successful thoracoplasty This latter consideration still influences many of our patients in favor of extrapleural pneumothorax The remainder of the procedures in this particular classification were performed chiefly in females because of cosmetic considerations

*Combined Immediate Postoperative Results of all Extrapleural Procedures* (Table IV) In all of the 148 procedures there were only 3 operative deaths or a mortality rate of 2 per cent Two of these deaths occurred in hopeless cases while the third was the result of an immediate postoperative accident The immediate operative results were highly successful in 129 instances or 87.2 per cent while the operation was a failure in 16 instances or 10.8 per cent of the total As a result of our added experiences with this procedure, the incidence of operative failure has been reduced to a negligible minimum in recent years Most of the failures occurred early in the series when we were not able to recognize the unfavorable cases prior to surgery Aside from other more general considerations, we consider very dense disease, pachypleuritis, and large subpleural cavitation as definite contraindica-

TABLE IV  
*Combined Immediate Postoperative Results of all  
Extrapleural Procedures*

Classification	Group Followed	Group Not Followed	Total	Per Cent
Successful	95	34	129	87.2
Operative Failure	8	8	16	10.8
Operative Death	1	2	3	2.0
Total	104	44	148	100.0



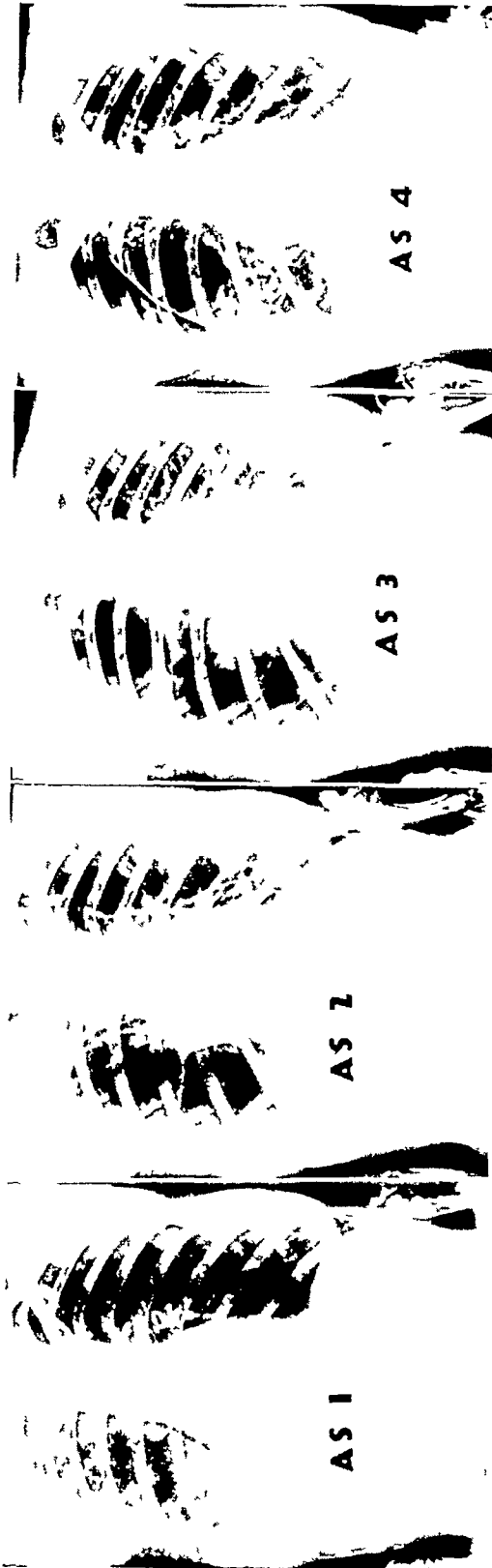


FIGURE 6 A S , a 28-year-old white female Very extensive disease on the right side (1) Intrapleural pneumothorax failed to control apical disease (2) Combined intrapleural and extrapleural pneumothorax established 4-4-40 (3) Eighty-six months later patient's disease is arrested (4) Has since given birth to healthy child and does all her own housework

tions to extrapleural pneumothorax since they predispose to serious operative and postoperative complications (figures 8 and 9)

*Analysis of Long Term Results in 88 Patients Followed\** (Table V) This particular analysis is confined to the 88 patients in whom the 95 immediate operative and postoperative results were successful (Table IV) These cases were observed for periods of time ranging from 12 months in some instances to almost 8 years in others For expediency and simplification the long term results in these 88 patients have been arbitrarily classified as good, fair and poor Sputum conversion, retrogression of the pulmonary disease and improvement in the patient's general condition are the criteria for a good result On this basis 43.3 per cent of the hopeless patients and 64.6 per cent of all the remaining cases obtained good results If the pulmonary disease remains stationary after operation with or without sputum conversion or general improvement, the result was considered fair Ten per cent of the hopeless cases and 8.5 per cent of the remaining patients had only fair results by these standards The result was considered poor if the pulmonary lesion showed signs of progression following surgery or if the patient's general condition continued to deteriorate Poor results were obtained in only 6.7 per cent of the hopeless cases as compared to 11.9 per cent of all the remaining cases The apparent discrepancy in favor of the hopeless group is nullified when one considers the fact that 40 per cent of the hopeless patients died during the period of observation as compared to only 15 per cent fatalities in all other cases followed The important observation in this particular analysis, however, is the fact that 18 patients representing 60 per cent of the hopeless group followed are still alive today and more than 70 per cent of

\*Does not include 8 operative failures and 1 operative death

TABLE V  
*Analysis of Long Term Results in 88 Patients Followed\**

Results	Hopeless Cases		All Other Cases		Total Cases	
	No	Per Cent	No	Per Cent	No	Per Cent
Good	13	43.3	38	64.8	51	58.0
Fair	3	10.0	5	8.5	8	9.0
Poor	2	6.7	7	11.9	9	10.2
Total Living	18	60.0	50	85.0	68	77.2
Total Dead	12	40.0	8	15.0	20	22.8
Total	30	100.0	58	100.0	88	100.0

\*Does not include 8 operative failures and 1 operative death

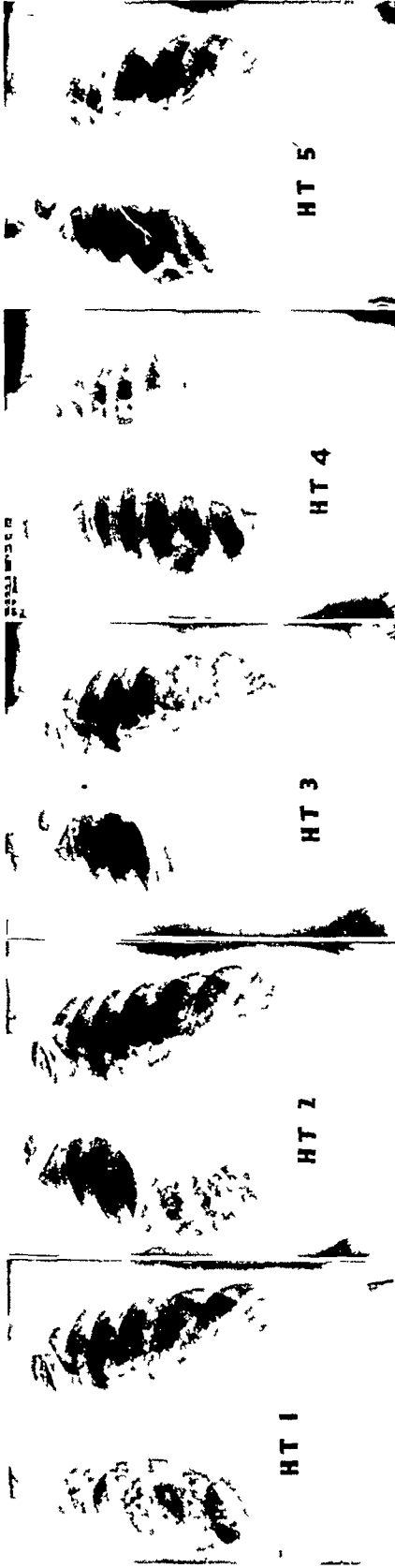


FIGURE 7 H T a 45-year-old white female Far advanced disease and hopeless general condition Right and left intrapleural pneumothorax failed (1) First stage extrapleural pneumothorax performed 4-11-41 (2) Disease subsequently spread to right base and continued to spread in left side (3) Condition unfavorable for thoracoplasty Second stage extrapleural pneumothorax on 1-2-42 (4) Two years later the right side was making satisfactory progress but hemorrhage from left lung was fatal (5)

these show signs of continued improvement and possible eventual arrest of the disease. If left on their own resources, there would unquestionably have been more than 12 deaths in the hopeless group at the time of this survey. Furthermore, 50 or 85 per cent of the group not classified as hopeless are alive today. Of these, 38 or more than 75 per cent show definite signs of continued improvement and hope for eventual arrest of the disease. The results of extrapleural pneumothorax therapy in this latter group compare most favorably with the results achieved by other more acceptable and widely-practiced measures of collapse therapy. Since 1944 there has not been a single death in the combined groups. During this time 23 operations were performed. Most of the fatalities prior to 1944 occurred during 1940 and 1941. These deaths were predominantly in the hopeless group and were more than likely the results of our own inexperience or unwise selection of the early cases in this series for surgery (figures 8 and 9).

*All Complications Encountered in 104 Extrapleural Procedures* (Table VI). Postoperative, sero-sanguinous fluid of varying amounts occurred in 100 per cent of the cases (figures 2, 4 and 5). It was usually harmless and with proper management was completely resorbed within one month following surgery. In a few instances, the fluid persisted for longer periods of time and some of these cases subsequently developed empyema. Emphysema was

TABLE VI  
*All Complications Encountered in 104 Extrapleural Procedures*

Type	Number	Per Cent
Postoperative fluid	104	100.0
Emphysema	4	3.8
Empyema	13	12.5
Bronchopleural fistula	5	4.8
Lipoid pneumonia	1	0.9
External fistula	4	3.8

TABLE VII  
*Analysis of Empyema and Bronchopleural Fistula Cases*

Method of Maintaining Collapse	EMPHYEMA CASES		BRONCHOPLEURAL FISTULA CASES	
	No.	Per Cent	No.	Per Cent
Air (75 per cent)	8	61.6	1	20
Oil (25 per cent)	5	38.4	4	80
Total	13	100.0	5	100

an unimportant complication in 4 instances following surgery and required no special treatment (figure 5) Perfection of the operative technique has almost eliminated this minor and transient complication in recent years Empyema, however, is by far the most important complication (figures 8 and 9) It occurred in 13 or 12.5 per cent of the cases In 9 instances it was associated with 2 other serious complications, bronchopleural or external fistulae The long term results in those patients who developed empyema or any of the other serious complications were, with few exceptions, uniformly poor One patient accidentally developed a lipid pneumonia following an unsuccessful attempt to fill the extrapleural space with oil After a stormy course, this patient subsequently made an uneventful recovery from this complication

*Analysis of Empyema and Bronchopleural Fistula Cases* (Table VII) In this series, approximately 75 per cent of the extrapleural spaces were maintained with air while, at one time or another, about 25 per cent were maintained with oil Of the 13 instances of empyema, 61.6 per cent occurred in the group maintained with air while 38.4 per cent occurred in the group maintained with oil Bronchopleural fistula occurred in only one case maintained with air while it was a complication in 4 cases maintained with oil Although this is an admittedly limited study from which to draw any rigid conclusions, one is nevertheless impressed by the greater frequency of empyema and bronchopleural fistula as



FIGURE 8 V W, a 32-year-old white female Very dense apical disease and pachypleuritis Intrapleural pneumothorax failed (1) Following surgery he developed purulent empyema which required a thoracotomy (2) Patient is alive today following thoracoplasty

complications in the group maintained with oil. As a result of these findings, we reserve extrapleural oleothorax for very special and rare occasions and avoid its use whenever possible.

*Discussion* After careful evaluation of the statistical results obtained in this series of patients, we are satisfied to conclude that extrapleural pneumothorax is a very valuable form of temporary collapse therapy in the treatment of pulmonary tuberculosis. In fact, the results by comparison are as good, or better, than those obtained with other more generally practiced forms of collapse therapy. Our conclusion is, nevertheless, not in agreement with the majority of opinions expressed in the recent American literature. Perhaps the almost uniformly poor results reported by these investigators following their use of extrapleural pneumothorax reflects their inexperience with this particular type of procedure and poor choice of patients rather than a condemnation of this particular form of therapy. An unbiased evaluation of our earlier results clearly demonstrates and supports the latter observation. As our selection of patients, surgical technique and proficiency in the satisfactory maintenance of extrapleural space improved, so did our results. In many of these reports this procedure was used as a last resort in only hopeless cases when all other forms of therapy had failed or were not practicable. How, therefore, is it possible to equitably evaluate their results obtained with extrapleural pneumothorax on the same basis as the results

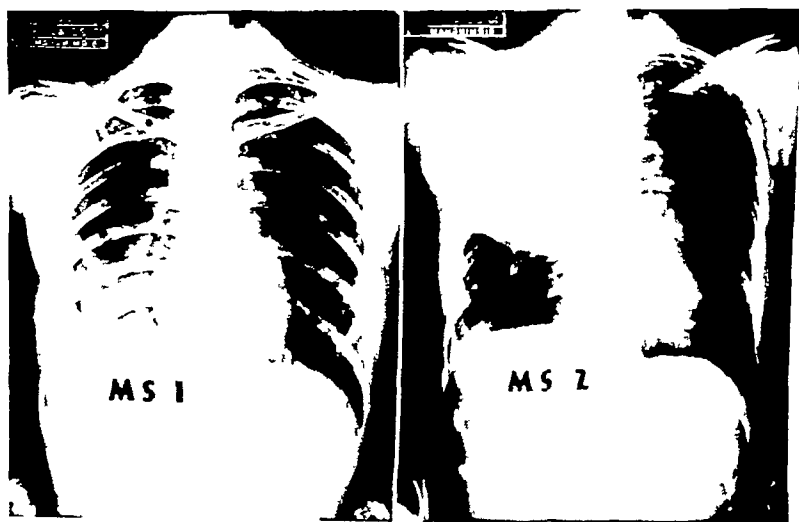


FIGURE 9 M S a 31-year-old white female. Unsuccessful intrapleural pneumothorax and large subpleural cavity on right side (1). During Surgery (6-40) accidental communication between extrapleural and intrapleural space established. Developed a purulent empyema and died 10 months later (2).

obtained with other forms of collapse therapy which usually were tried earlier and in more favorable cases

It is true that in many cases the maintenance of a therapeutic extrapleural collapse is much more difficult and requires more painstaking effort than that involved in intrapleural pneumothorax therapy. The beneficial results which one can expect from a satisfactory extrapleural collapse more than justify this effort. A relatively larger number of the failures, poor results, serious complications and deaths recorded in this survey occurred in those patients whose follow-up treatment was entrusted to less experienced hands after discharge from the sanatorium. As a result of our unfortunate experience with extrapleural oleothorax (Table VII), we are not in a position to recommend its routine use as a solution to the difficult problem of maintaining an effective extrapleural space in the postsanatorium period of treatment. On the other hand, these disadvantages have been overcome to a large degree by treating out-patients ourselves or by teaching physicians in outlying districts how to administer air refills at proper intervals under our close supervision. In this connection, one may recall similar difficulties encountered in patients treated with intrapleural pneumothorax. On a comparative basis, the relatively simple surgical procedure involved in the production of an extrapleural space is not nearly as important in the ultimate prognosis as intelligent follow-up treatment. After the extrapleural space is established at surgery, its careful development and maintenance in the immediate postoperative period is an essential prerequisite for the ultimate success of the procedure. Spontaneous reexpansion is no more frequent than in an intrapleural pneumothorax if the case is followed and managed properly. Reexpansion, when indicated, is generally accomplished with ease and rapidity, although usually accompanied by a very dense pleural reaction (figure 5).

The selective nature of the collapse and absolute lack of surgical shock makes extrapleural pneumothorax the collapse procedure of choice for patients in the older age group and for those in poor general condition. Its interference with physiologic pulmonary function is minimal and much less than all other methods of collapse therapy. Therefore, it can be utilized in those patients who already have impaired pulmonary function as evidenced by a lowered vital capacity. Similarly, it can be used as a temporizing measure when the occasion warrants in preparation for a future thoracoplasty on the ipsilateral or contralateral side. In the presence of scattered apical disease we feel that an extrapleural pneumothorax is actually preferable to thoracoplasty provided there is no cavity larger than 4.5 cm. and that total cavitation

is not excessive. The so-called hilar cavity is frequently benefited by this form of therapy since it is more accessible to direct collapse. We also reserve this procedure for those patients who refuse to submit to thoracoplasty either because of fear or cosmetic considerations. Although the latter utilization of extrapleural pneumothorax has no valid medical basis, nevertheless, it is better than no treatment at all in the uncooperative patients. We, further, are of the opinion that extrapleural pneumothorax is especially designed for communities with limited sanatorium facilities. It can be accomplished without undue danger to the patient in the presence of limited surgical and nursing facilities since it is a much simpler and less shocking procedure than thoracoplasty. In addition, the period of convalescence and rehabilitation of the patient is generally more rapid.

The foregoing comments clearly indicate our position in regard to extrapleural pneumothorax as a form of temporary collapse therapy in pulmonary tuberculosis. We wish to emphasize, however, that this form of therapy is not offered as a panacea or substitute for all other forms of collapse therapy but rather as an acceptable and valuable additional therapeutic measure to supplement the phthisiologist's manifestly inadequate and unsatisfactory armamentarium.

### SUMMARY

1) A statistical analysis of the results achieved with extrapleural pneumothorax over an eight year period has been presented and discussed.

2) After careful evaluation of this survey of our experiences, we are satisfied to conclude that extrapleural pneumothorax is a very valuable form of temporary collapse therapy in the treatment of pulmonary tuberculosis.

### RESUMEN

1) Se presenta y discute un análisis estadístico de los resultados obtenidos en un período de ocho años con el neumotórax extrapleural.

2) Después de evaluar cuidadosamente nuestra experiencia, estamos satisfechos de que podemos sacar la conclusión de que el neumotórax extrapleural es una forma muy valiosa de la colapso-terapia temporaria en el tratamiento de la tuberculosis pulmonar.

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## D I S C U S S I O N

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We have operated on 17 patients (one had bilateral operation) Eight of these were done in 1938-41, 9 in 1945-46 In the first group 3 had empyema, 6 eventually died, 2 are living and well, one of which had good air refills for four years and the lung reexpanded subsequently without difficulty Of the 9 in the second group, 2 had contralateral thoracoplasty One developed an empyema necessitans that is clearing In 7 patients the air was replaced with gomenol oil All cavities remain apparently closed, the sputum was converted in 8 cases and to date there has been no mortality

Although the numbers are small and the second group only one year old, it is interesting to note the strikingly different results obtained in the two groups The same technique was used in both groups This illustrates the varied results reported by different clinics on the same operative procedures The range of indications appear to be the determining factor As with most new operations there has been a tendency to try the bad cases first, naturally results are also bad In the first group nearly all were hopeless bilateral cases, while the second group did not include the more widespread subacutely progressive cases Here some antibiotics may be used advantageously in an attempt to stabilize the lesions prior to other anticipated operative interferences The majority of the patients in the second group had bilateral cavities, few others, especially women, refused thoracoplasty

The late progressive loss of the extrapleural pocket and the incidence of empyema seem to be reduced when 1) Bleeding is carefully controlled at operation, blood clots are removed even by open approach if necessary 2) Pre and postoperative use of antibiotics such as penicillin (Streptomycin should prevent most of the tuberculous empyemas) 3) The extrapleural pocket is blocked early by oil (4-6 weeks postoperative), at a time when the size of the pocket seems to be optimal Oil pressure readings are taken at regular intervals Results seem to be encouraging We intend to try more cases and over longer periods of observation

An extrapleural pneumonolysis with contralateral thoracoplasty is preferred to bilateral thoracoplasty, respiratory function is less disturbed At first the extrapleural is done on the more recent and less extensive side Later the thoracoplasty is done on the other side the size being accommodated to the extent and position of the lesions, and the respiratory reserves of the patient

# Relationship of the Pleural Fluid Sugar to Pulmonary Tuberculosis

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Because of the characteristic low sugar content of the spinal fluid in cases of tuberculous meningitis, it was decided to study this phenomena in pleural effusions, in an effort to determine the relationship, if any, of tuberculous pleural effusion and the pleural fluid sugar

Up to the present time the only work reported along this line was that of E Nassau He found that those cases of exudative pleurisy with a positive tubercle bacillus culture had a sugar content between 15 and 84 mgs per cent, with an average of 49.25 mgs per cent, as compared with a range of 80 to 132 mgs per cent and an average of 115.16 mgs per cent in the negative bacilli cases He further discovered that in pneumothorax pleurisy the sugar ranged from 63 to 136 mgs per cent, with an average of 88.5 mgs per cent in the negative bacilli cases, whereas in the tubercle bacillus positive cases the sugar determination fell between 4 and 92 mgs per cent, averaging 44.46 mgs per cent In tuberculous empyema the sugar varied from 7 to 22 mgs per cent, with the average at 12.4 mgs per cent

## *Procedure*

A total of 33 cases of pleural effusion comprises the series Comprehensive histories were taken and complete physical examinations were given each patient Routine blood and urine studies as well as chest x-ray films were made In cases where indicated, other procedures such as biopsy, sputum and bronchoscopic examinations were done

The fluid removed from the chest was subjected to the following tests specific gravity, total protein, cell count, total sugar, stained smear, culture, and guinea pig inoculation A venous blood sugar was drawn at the same time for comparison with the pleural fluid sugar

Many of the cases required repeated examinations of the pleural fluid in order to establish the diagnosis However, for purposes of standardization only the original sugar determination was used

Sugar determinations on the subsequent thoracenteses tended to approximate closely the original determination

Sugar determinations were made by the Folin-Wu method using a photo-electric colorimeter. The pleural fluid was concentrated by Petrof's method and cultured on Petraghani's medium and inoculated into the inguinal lymph nodes of two guinea pigs which were autopsied at three and eight weeks respectively.

We were able to establish the etiology of 31 of the 33 cases. The remaining two cases failed to reveal the cause of the effusion after an extensive search.

## R E S U L T S

### GROUP 1—8 CASES

Tuberculosis	8
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### GROUP 2—4 CASES

Tuberculosis	2
Bronchogenic carcinoma	1
Unknown	1

### GROUP 3—21 CASES

Post pneumonic	9
Primary bronchogenic carcinoma	3
Traumatic	2
Metastatic malignancy to lung	2
Carcinoma of stomach	1
Metastatic abscess to lung	1
Spontaneous pneumothorax	1
Congestive heart failure	1
Unknown	1

On the basis of the amount of sugar in the pleural fluid, all the cases could be divided into three general groups:

*Group 1* Those with a pleural fluid sugar below 30 mgs per cent

*Group 2* Those with a pleural fluid sugar between 30 and 60 mgs per cent

*Group 3* Those with a pleural fluid sugar above 60 mgs per cent

There were eight cases in Group 1 where the sugar ranged from a trace to 25.1 mgs per cent. The average of this group was 10.9 mgs per cent. At the same time the venous blood sugars varied from 82 to 142 mgs per cent. In every one of the eight cases tubercle bacilli were demonstrated either by culture or guinea pig inoculation of the pleural fluid. Many required repeated search for the organisms, which sooner or later were found. In none of these cases was there x-ray evidence of tuberculosis.

In Group 2 there were four cases. The pleural fluid sugars varied from 30.3 to 39.5 mgs per cent, averaging 36.3 mgs per cent. The venous blood ranged from 104 to 122 mgs per cent. In two of the four cases tuberculosis was subsequently diagnosed. One patient

had a bronchogenic carcinoma, while the fourth failed to reveal the cause of the effusion. The latter has been followed for a period of two years without developing subsequent complications.

Group 3 consisted of 21 cases, all of which had a pleural fluid sugar between 62 and 140 mgs per cent. Venous blood determinations fell between 79 and 166.7 mgs per cent. Tuberculosis was not found to be present in any of this group. After appropriate study, the cause of the effusion was found in all except one case. The greatest majority were post-pneumonic in origin. There were nine such cases. The effusion accompanied primary carcinoma of the lung in three instances. Two were traumatic. Likewise, two resulted from metastatic growths in the lungs. There was one case each of congestive heart failure, carcinoma of the stomach, metastatic lung abscess, and spontaneous pneumothorax with pleural effusion. Repeated examinations of one patient failed to disclose the cause of the effusion. This case has been followed for six months, and up to the present time there have been no further developments.

### *Conclusions*

We hesitate to draw specific conclusions from this small series of cases, but it seems very probable that the determination of the pleural fluid sugar may be quite useful diagnostically in the obscure sero-fibrinous pleural effusions.

The lower the sugar level the greater the possibility of tuberculosis. All of the cases of tuberculosis had a level below 39.5 mgs per cent. The average sugar determination of all cases of tuberculosis was 15.7 mgs per cent. A finding of 30 mgs per cent or less should be considered diagnostic of tuberculosis and should be followed by an intensive search for the organism.

Cases with borderline values of pleural fluid sugar should be considered as tuberculous until proved otherwise.

If the sugar level is above 60 mgs per cent it is quite unlikely that the cause of the effusion is tuberculosis.

### *SUMMARY*

A series of 33 cases of pleural effusion were studied, as to the sugar determination of the pleural fluid. The sugar findings fell into three groups.

Group 1 those with a sugar determination below 30 mgs per cent (8 cases). Group 2 those between 30 mgs and 60 mgs per cent (4 cases). Group 3 those above 60 mgs per cent (21 cases).

All the Group 1 cases were found to have tuberculosis. Two of the Group 2 cases had tuberculosis. The rest had some other

TABLE 3

Admission Diagnosis	Number of Cases	History of Contact	Asymptomatic	Chronically Ill	Acutely Ill	Afebrile	Febrile	Positive Tubercu- lin Test	Gastric Washings Positive for Acid-fast	Tuberculous Com- plication after admission	Non-tuberculous Complications	Re-Admissions with Tuberculous Complications	Deaths
Primary Tuberculous Infection	186	138	167	17	2	166	20	165	38	6	23	3	2
Pleurisy with Effusion	21	11	15	5	1	18	3	20	8	0	2	0	1
Miliary Tuberculosis	14	7	7	1	6	6	8	9	5	5	2	0	7
Re-infection Tuberculosis	7	6	2	3	2	3	4	6	6	2	1	1	1
Non-tuberculous	5	2	3	1	1	2	3	0	0	0	0	0	0
Tuberculous Meningitis	1	1	0	0	1	0	1	1	0	0	0	0	1
TOTAL	234	165	194	27	13	195	39	201	57	13	28	4	12

*Case 3* A six year old colored girl was admitted in May 1942. The tuberculin test was positive and a definite history of contact was obtained. The patient was afebrile and symptom free on admission, and physical examination revealed no abnormal findings. Chest x-ray film revealed an active primary infection. Tubercle bacilli were demonstrated on guinea pig inoculation. Shortly after admission the patient became acutely ill and a repeat chest x-ray examination showed a miliary dissemination of the disease and the patient developed signs and symptoms of meningitis. The patient died on the sixty-ninth hospital day of tuberculous meningitis.

*Case 4* A seven year old colored male was admitted in July 1943 with a history of contact. The tuberculin test was positive. The patient ran a persistent low grade fever but otherwise did not appear ill. Admission chest x-ray film revealed an active primary infection. Physical examination revealed no abnormal findings. Gastric washings were positive for acid-fast bacilli on guinea pig inoculation. The patient developed right pleurisy with effusion four weeks after admission. This gradually cleared without further complications and the patient was discharged after 338 days in the hospital.

*Case 5* A five year old colored boy was admitted in April 1943 with sickle-cell anemia and primary tuberculosis. He had a definite history of contact and the tuberculin test was positive. The patient was acutely ill on admission and ran a persistent spiking fever. He required frequent blood transfusions for his severe anemia. The patient ultimately developed tuberculosis of the spine. Gastric washings were negative for acid-fast bacilli. The patient died of sickle-cell anemia after 1,416 days in the hospital.

*Case 6* An eighteen month old white male was admitted in August 1947. No history of contact was obtained, but the tuberculin test was positive. The patient was chronically ill, listless and ran a persistent fever as high as 102 degrees F. Admission chest x-ray film revealed an active primary infection with a large patch of parenchymal infiltrate on the right. Although all signs and symptoms abated and the temperature returned to normal, a repeat chest x-ray examination showed a definite spread of the initial pulmonary lesion. Gastric washings were positive for acid-fast bacilli on guinea pig inoculation. Serial x-ray examinations showed gradual clearing of the pulmonary lesion without further complications.

Three patients (11 per cent) were re-admitted to the hospital for tuberculous complications which developed after discharge. One was the nine year old colored girl who ultimately died of tuberculous meningitis. The other two were children who were discharged with a diagnosis of a retrogressive primary infection, both of whom were re-admitted within thirty days after discharge with pleurisy and effusion. Both patients recovered without further complications.

To summarize then, there were nine children (4.4 per cent) who developed tuberculous complications out of the group of 186 patients originally admitted with a diagnosis of primary tuber-

culosis Six of these complications developed while the patients were still in the hospital, and three patients developed complications after medical discharge from the hospital which were severe enough to require re-admission There was a definite history of contact in eight of the nine patients, and acid-fast bacilli were demonstrated in six out of the nine cases The tuberculin test was positive in all nine patients Six of the children were febrile or presented symptoms of illness on admission to the hospital, while three were entirely afebrile and symptom-free on admission

There were twenty-eight children (11.9 per cent) who developed non-tuberculous complications after admission to the hospital Twenty-six of these were acute contagious diseases, there was one patient who developed a non-specific corneal ulcer, and one patient fractured his arm falling out of bed

The hospital stay in days for children with a primary infection ranged from a minimum of twelve days to a maximum of 1,416 days, with an average of 250 days per patient Treatment on the childrens ward consists of general supportive care The children are kept in bed at all times When they become too active in the judgment of the nurses on the floor, restraining jackets are used Those children who are of school age go to and from the classroom on the ward in a wheel-chair, and attend classes for one hour daily All of the children take a two and a half hour nap daily They receive a 2000-2200 calorie diet and are given cod-liver oil and Feosol daily None of the patients with a primary infection have received specific therapy in any form Streptomycin has not been used at this hospital for the treatment of primary tuberculosis Serial chest x-rays are taken every two months routinely Children are usually not considered ready for discharge until there has taken place complete absorption of the parenchymal lesion, and contraction or calcification in the regional lymph nodes All cases for discharge are presented before the entire hospital staff in a manner similar to the routine with adult patients

### *Comment*

From this study, it is evident that the overwhelming majority of children with a primary infection do well with no specific therapy The trend in recent years has definitely been away from the special care which these patients formerly received In the final analysis, hospitalization of these patients offers just one advantage, and that is the opportunity to diagnose a tuberculous complication in its early stages With the clinic care which is now available, this responsibility could be taken over by the clinics Then too, the emotional stress which is placed both upon the

parents and the child by long term hospitalization is sufficient in itself to contra-indicate this type of care unless absolutely necessary

A more critical evaluation of patients with a primary infection seems indicated with respect to long term hospitalization. Assuming that only those children with a positive tuberculin test and chest x-ray evidence of an active primary infection would be candidates for hospitalization, admissions should be limited to those patients who satisfy the following criteria

- 1) A definite history of contact, preferably in the immediate family group, where the exposure is intimate
- 2) The presence of acid-fast bacilli in the gastric washings on repeated examinations at monthly intervals
- 3) Clinical symptoms of illness and fever
- 4) Definite progression of the pulmonary lesion on chest x-ray examination
- 5) The development of tuberculous complications, either pulmonary or extrapulmonary

#### SUMMARY

1) There were 234 patients admitted to the hospital between January 1, 1942, and December 31, 1947. There was no significant variation in the age, race, or sex of the patients admitted.

2) One hundred and eighty-six (79.5 per cent) of the patients were diagnosed on admission as having primary tuberculosis. Of this group, 167 (89.8 per cent) were asymptomatic, and 166 (89.3 per cent) were afebrile on admission. Acid-fast bacilli were demonstrated in 38 patients (20.4 per cent).

3) Six children (3.3 per cent) admitted with a primary infection developed tuberculous complications after admission to the hospital. Three children (1.1 per cent) required readmission to the hospital, after medical discharge for tuberculous complications. Eight of these patients had a definite history of contact, and tubercle bacilli were demonstrated in six of these patients. Six children had clinical symptoms of illness or fever, while three were afebrile and asymptomatic, prior to the development of their tuberculous complications.

4) Treatment consisted of bed rest and an adequate diet. No specific therapy was instituted in any case with a primary infection. The average hospital stay for patients with a primary infection was 250 days.

#### RESUMEN

1) Se admitieron a 234 pacientes al hospital desde el 1o de enero de 1942 al 31 de diciembre de 1947. No hubo variación significativa en la edad, raza o sexo de los pacientes admitidos.



2) Se hizo el diagnóstico de tuberculosis primaria en 186 (79.5 por ciento) de los pacientes admitidos. De este grupo, 167 (89.8 por ciento) eran asintomáticos y 166 (89.3 por ciento) no tenían fiebre cuando fueron admitidos. Se demostraron bacilos ácido-resistentes en 38 pacientes (20.4 por ciento).

3) Seis niños (3.3 por ciento) admitidos con una infección primaria desarrollaron complicaciones tuberculosas después de haber sido admitidos al hospital. Tres niños (1.1 por ciento) necesitaron readmisión al hospital debido a complicaciones tuberculosas después de haber sido dados de alto. Ocho de esos pacientes presentaron una historia de contacto bien definido y se demostraron bacilos tuberculosos en seis de ellos. Seis niños tenían signos clínicos de enfermedad o fiebre, mientras que tres no tenían fiebre u otro síntoma, con anterioridad al desarrollo de las complicaciones tuberculosas.

4) El tratamiento consistió de reposo en cama y dieta adecuada. No se empleó terapia específica en ningún caso de infección primaria. El promedio de la estancia en el hospital de los pacientes con la infección primaria fue 250 días.

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# Pathologic Aspects of Atypical Pneumonias

## (Interstitial Pneumonitis)

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In this discussion of interstitial pneumonitis, (or interstitial pneumonia, atypical pneumonia), it is intended to present certain aspects of the underlying pathologic changes in both common and unusual types of atypical pneumonias. Very many and very diverse injurious agents can and do injure the tissues of the lung and cause inflammatory reaction and disease. The lung tissues, however, have a limited reactive capacity, or a limited number of ways in which they can react to the diverse injurious agents. The pneumonias produced are anatomically classified as lobar, lobular or broncho—, and interstitial (commonly called interstitial pneumonia or interstitial pneumonitis).

Interstitial pneumonitis is characterized by the fact that in inflammatory reaction and inflammatory exudate is found predominantly in the interstitial tissues, the supporting framework of the lung (in bronchioles, peribronchiolar tissues, and alveolar walls), rather than in alveolar spaces. Also, characteristically, the cells of the inflammatory exudate tend to be predominantly of mononuclear types, rather than neutrophilic polymorphonuclear leucocytes. In certain varieties of interstitial pneumonia, the epithelial lining cells of bronchioles and of alveoli show peculiar changes. Sometimes interstitial pneumonitis is accompanied or followed by a progressive fibrosis.

In general, one can say that this interstitial type of pulmonary change most often is a reaction to injury by microorganisms which live and grow only within living cells—viruses, rickettsiae, certain protozoa, such as toxoplasma, and certain types of fungi, such as histoplasma. The higher bacteria, which are capable of growth without the enzyme systems found in living cells, only uncommonly cause this type of reaction. One could speculate with considerable interest about reasons why microorganisms which prefer to be or are obliged to be intracellular in their parasitism, elicit a certain type of response on the part of the pulmonary tissues.

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### *Influenzal Pneumonia*

Studies of the pandemic of influenza during and after World War I, indicated that in cases in which death occurred during the first five days of illness, the pulmonary lesions were an interstitial pneumonitis similar to that found in the current atypical pneumonia. When the clinical duration was greater than one week, secondary bacterial infection with streptococci, pneumococci or other organisms was the rule, and some variety of a bronchopneumonia or lobar pneumonia resulted. These studies, and also experimental studies on influenza in swine, lead to the conclusion that influenza, uncomplicated by secondary bacterial infection, is characterized by a pulmonary lesion of acute interstitial pneumonitis.<sup>1 2</sup>

#### *Acute Interstitial Pneumonitis, Etiology Undetermined* (Atypical Pneumonia)

Most details about the atypical pneumonia which has been prevalent now for almost a decade are quite familiar. The etiology, although presumably viral, still lacks complete proof. The mortality in uncomplicated cases has been very low, so that few pathologists have had an opportunity to study more than a few isolated cases. Reimann,<sup>5</sup> in a review published in May 1947, stated that only about 20 necropsy reports were available and that many of these were incomplete. However, the unparalleled opportunity provided by the central pathologic laboratory of the United States Army, made more than 42 cases available in one series.<sup>3</sup> Parker, Joliffe and Maxwell<sup>16</sup> have recently reported on eight necropsied cases. From published reports and personal experience a composite description of the pulmonary lesion may be given.

The lungs are slightly or moderately increased in weight. The pleural surfaces are usually smooth and glistening, but occasionally there are patches of fibrinous pleurisy. Pleural effusion is unusual. The extent of lung involvement varies from a portion of a lobe, to a whole lobe, a whole lung, or a diffuse bilateral spread. Focal, slightly-raised, whitish areas on the cut surface are involved bronchioles, which contain a thick mucopurulent material. Surrounding tissue is congested, and sometimes edematous or hemorrhagic.

Microscopic sections of the larger and medium-sized branches of the bronchial tree show intact mucosa, with marked submucosal edema, congestion, and infiltration by mononuclear cells. Involved bronchioles, which have a spotty distribution, show characteristic changes. The lumens contain a mixture of pus,

desquamated mucosa, and mucoid fluid. The bronchiolar mucosa is ulcerated. The walls are thickened, often markedly, by an abundant exudate of plasma cells, lymphocytes, monocytes and edema fluid. Neutrophilic leucocytes are scanty. The affected bronchioles are often dilated, the fibers of their walls being degenerated or fragmented. The cellular and fluid exudate extends radially into peribronchial tissues and adjacent alveolar walls. Affected alveolar walls may be thickened to several times their normal dimensions, but are not ruptured or necrotic. The alveolar spaces may be air-containing, atelectatic, or may contain serous exudate with a few mononuclear cells. The serous exudate often is crowded to the periphery of the alveolar space, forming a hyaline membrane. Microorganisms may be demonstrable in bronchiolar lumens, but are absent elsewhere in the involved tissue.

Metaplasia of lining epithelial cells is quite a common finding. Bronchiolar lining cells may show a focal or more diffuse metaplasia to a squamous type, and alveoli also may show a lining of metaplastic epithelial cells of columnar type, or even squamous areas.

In some cases pleurisy may be present. A thin layer of fibrin without leucocytes is present on the surface. The subpleural tissues are edematous, congested, and infiltrated by monocytes, lymphocytes, and plasma cells.

Such is the basic picture of interstitial pneumonitis. The various conditions to be described are but variations of this picture in which certain features are prominent and others subdued. A number of conditions in which a viral origin has been more conclusively demonstrated give a similar or indistinguishable picture. Psittacosis and other forms of ornithosis are examples, although they are known to account for but a very small proportion of clinical cases of atypical pneumonia. Q fever, at one time thought to be due to a viral organism, but now usually classed as a rickettsia, also has a very similar clinical and pathologic picture.

### *Rickettsial Pneumonitis*

Various rickettsial diseases may have, among other tissue involvements, an interstitial pneumonitis which in its essentials is the same as that of atypical pneumonia. This occurs almost invariably in Q fever, in about half the cases of tsutsugamushi disease (scrub typhus), and less frequently and with less severity in typhus fever and Rocky Mountain spotted fever.

The rickettsial interstitial pneumonitis, as exemplified by that seen in scrub typhus,<sup>6</sup> shows bronchiolar involvement, the lumens filled with purulent exudate mixed with mucous and desquam-

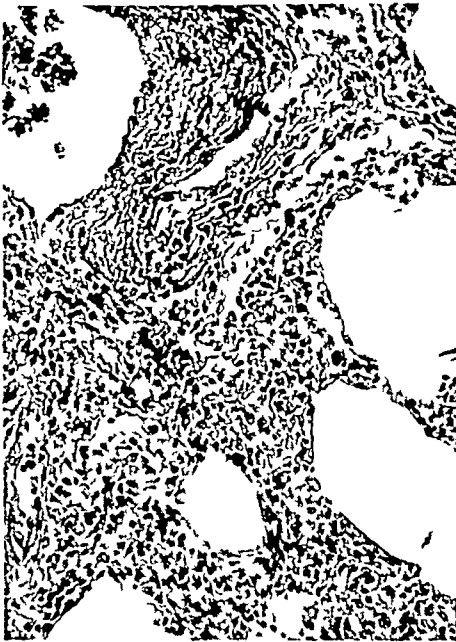


FIGURE 3



FIGURE 4

*Figure 3* Pulmonary histoplasmosis, showing interstitial pneumonitis —*Figure 4* Pulmonary histoplasmosis, showing numerous encapsulated histoplasma within the cytoplasm of proliferated mononuclear cells



FIGURE 1

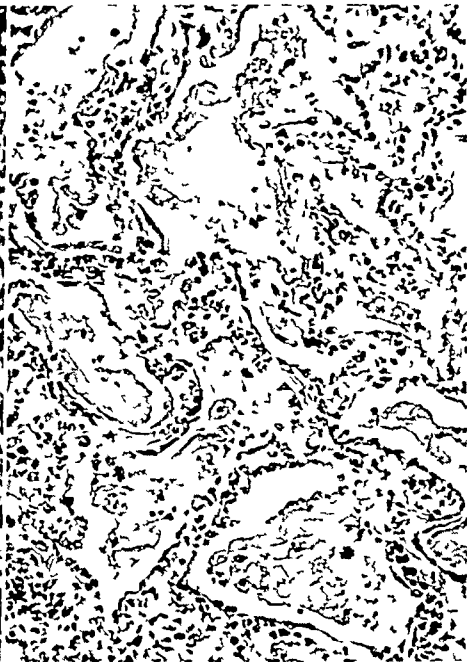


FIGURE 2

*Figure 1* Interstitial pneumonitis in scrub typhus. The alveolar walls are markedly thickened by edema and mononuclear exudate and alveolar lining cells are prominent (A I P neg No 82723) —*Figure 2* Toxoplasmic pneumonitis. Mononuclear exudate thickens alveolar walls. With higher magnification, toxoplasma may be identified in the prominent alveolar lining cells

ated epithelium. The bronchiolar epithelium is frequently partially eroded. The bronchiolar walls and adjacent radiating interstitial tissues are thickened by edema and infiltration by lymphocytes, plasma cells and macrophages. Alveolar lining cells become conspicuous, and in experimental animals rickettsiae have been observed in such cells. Evidence of fibroblastic proliferation in alveolar walls is common.

### *Toxoplasmic Pneumonitis*

Toxoplasma is a protozoan which recently has been recognized as the causative agent in certain types of meningo-encephalitis of newborn infants. The circumstances suggest prenatal infection, and hence imply latent infection in the mothers.

At least three cases of acute toxoplasmosis in adults have been recognized. They were characterized by a clinical picture similar to that of typhus or spotted fever, and the pathologic picture of interstitial pneumonitis. Death appeared to be due primarily to interference with respiratory function. The morphologic changes in the lungs are basically similar to the interstitial pneumonitis of atypical pneumonias. Important features, however, are a prominence of alveolar lining cells and a tendency to interstitial fibrosis.

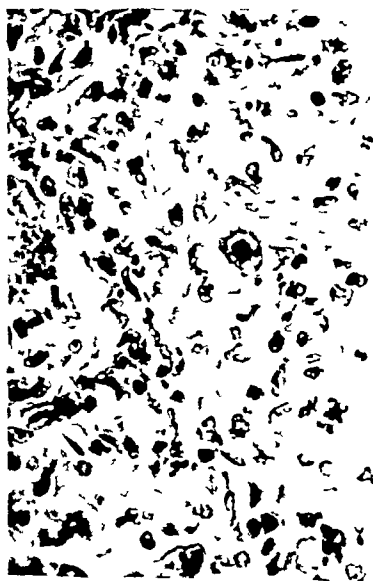


FIGURE 5



FIGURE 6

Figure 5. Pneumonitis in Inclusion Disease of Infancy. Note the large dark intranuclear inclusion and the predominance of mononuclear cells in the exudate.—Figure 6. Giant cell pneumonia of infancy. In addition to the thickening of alveolar walls by mononuclear exudate the hyperplastic alveolar lining cells have fused to form syncytial multinucleated giant cell forms.

Aveoli appear to be lined by cuboidal cells, in some of which the diagnostic toxoplasma may be found. The exudate of the alveolar septa tends to become organized, so that the thickened alveolar walls show early stages of fibrosis.

### *Histoplasmic Pneumonitis*

Histoplasmosis is due to an encapsulated yeast-like fungus. While occurring predominantly in the phagocytic cells of the reticulo-endothelial system, it has manifested itself on occasion as a respiratory infection.

In one case observed by the author,<sup>8</sup> in an infant, the most prominent manifestation was a respiratory infection which persisted four months until the time of death, and which at times received the clinical and roentgenological interpretation of tuberculosis and of bronchitis and bronchopneumonia. The lungs showed a patchy chronic pneumonitis, the irregular thickening of alveolar walls being due to increase of monocytes and fibroblasts. The diagnostic encapsulated "histoplasma" were recognizable in many of the monocytic cells. Unlike other types of interstitial pneumonitis, however, involvement of blood vessel endothelium was a

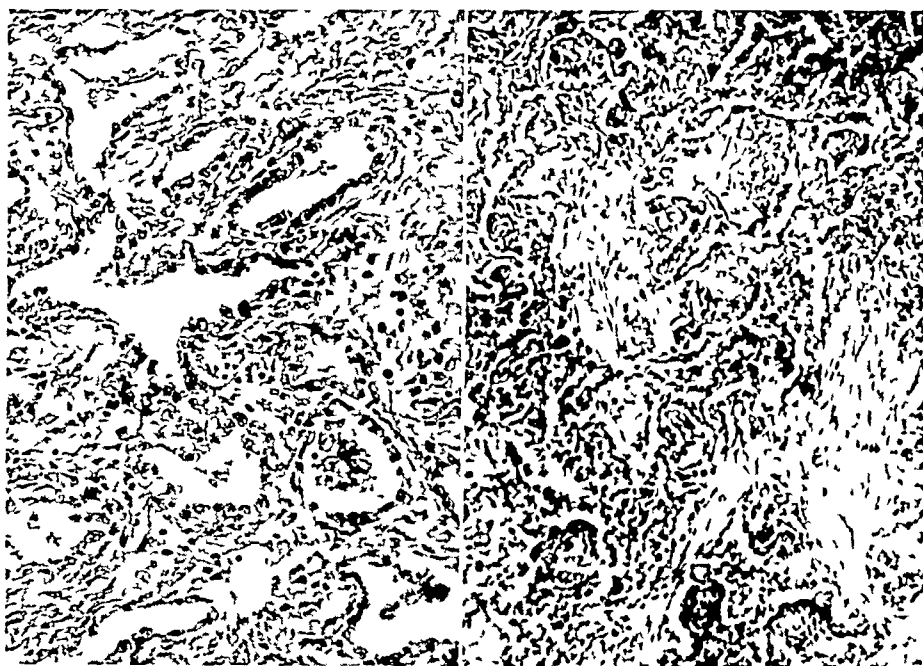


FIGURE 7

FIGURE 8

*Figure 7* Acute diffuse interstitial pulmonary fibrosis. The thickening of alveolar walls is due mainly to overgrowth of fibroblastic tissue, and cellular exudate is relatively scanty. The alveolar lining cells are prominent.—*Figure 8* Fibrosing or organizing pneumonia. In contrast to interstitial fibrosis, the fibroblastic overgrowth is the result of organization of exudate in alveolar spaces.

prominent and distinctive feature. In other cases of pulmonary histoplasmosis the histologic features have been more like those of tuberculosis or coccidiomycosis.

### *Viral Pneumonias of Infants and Children*

In several types of pneumonia in infancy distinctive inclusion bodies characteristic of viral activity have been found. The so called "inclusion disease" described by Farber and Wolbach<sup>9</sup> and others is characterized by an interstitial pneumonitis with prominent alveolar lining cells. Some of the lining cells show large granular inclusions which distend the nuclei, and occasional smaller cytoplasmic inclusions. An epidemic variety with a mortality of about 20 per cent has been reported by Adams,<sup>10</sup> in which only cytoplasmic inclusions are seen.

Giant cell pneumonia, as described by Hecht<sup>11</sup> in 1910, is a rare but distinctive interstitial pneumonitis. It is characterized by large multinucleated giant cells formed by proliferation and fusion of cells lining alveoli, alveolar ducts, and bronchioles. Cytoplasmic inclusions, pleomorphic and often very large, are found in these cases and also less numerous small nuclear inclusions.<sup>12</sup> The morphologic changes in the lungs, including the characteristic inclusions, are identical with those found in canine distemper in animals, and quite unlike that of any other known viral infection except early and uncomplicated measles pneumonia. This suggests a possible biological relationship of the viral etiology of giant cell pneumonia in man and canine distemper in animals. Also of particular interest is the fact that giant cell pneumonia is an interstitial pneumonitis in which the most prominent feature is a proliferation and metaplasia of alveolar and bronchiolar lining cells. This has features suggestive of the metaplastic changes in the respiratory tract found in Vitamin A deficiency.<sup>13</sup>

### *Acute Diffuse Interstitial Fibrosis of the Lungs*

In 1944, Hamman and Rich<sup>14</sup> described under the title "acute diffuse interstitial fibrosis of the lungs" a condition with unusual clinical and anatomical findings. It was characterized by a peculiar diffuse, progressive fibrosis of pulmonary alveolar walls, leading to deficient aeration of blood with resulting dyspnoea and cyanosis, and to enlargement and eventual failure of the right side of the heart. The alveolar walls were tremendously thickened but with little cellular exudate in comparison with the usual interstitial pneumonitis. The alveolar walls were edematous and crowded by fibroblasts, which in late stages matured to dense scar tissue. Other changes which were essentially similar



to those of the usual interstitial pneumonitis included enlargement of alveolar lining cells, necrosis of alveolar and bronchiolar epithelium, and formation of a hyaline membrane that lines alveoli Kneeland and Smetana,<sup>15</sup> in one of the early published reports on atypical pneumonia, included a case which was similar clinically and anatomically

### SUMMARY

The interstitial pneumonitis due to a variety of etiologic agents and circumstances has been commented upon to emphasize certain aspects not commonly stressed, namely, the common hyperplasia and metaplasia of alveolar and bronchiolar lining cells, and the tendency in many cases to progress to interstitial fibrosis The changes which often cause cyanosis to be a prominent clinical feature would merit a separate complete and full discussion One may speculate as to whether the present prevalence of atypical pneumonia may lead in the future to an increased clinical incidence of (1) effects of interstitial pulmonary fibrosis, and (2) pulmonary tumors resulting from stimulation of bronchiolar and alveolar lining cells Only time will give the answer

### RESUMEN

Se han discutido las neumonitis intersticiales debidas a una variedad de agentes y circunstancias etiológicas a fin de hacer énfasis sobre ciertos aspectos que comunmente no se recalcan, a saber, la hiperplasia y metaplasia comunes de las células alveolares y bronquiolares, y la tendencia de muchos casos de progresar a una fibrosis intersticial Las alteraciones que frecuentemente causan que la cianosis sea un rasgo clínico prominente merecen una discusión completa y separada Se puede meditar sobre la posibilidad de que la frecuencia actual de la neumonia atípica pueda conducir en el futuro a una creciente frecuencia clínica de (1) los efectos de la fibrosis pulmonar intersticial, y (2) tumores pulmonares debidos a la estimulación de células bronquiolares y alveolares Sólo el tiempo lo podrá decir

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# Routine Fluororoentgen Chest Examinations of Hospital Admissions

From the Viewpoint of the Radiologist\*

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The merits of chest surveys or screening by roentgen means cannot be disputed, provided adequate facilities and qualified professional personnel are available. The general principles governing such routine chest examinations, i e , hospital admission screening, mass surveys, pre-employment and pre-induction examinations, are not dissimilar. While it is not the primary intent nor within the province of the authors to discuss the latter three categories, consideration of a few of the general principles governing such extensive routine chest examinations is timely. Physicians, particularly roentgenologists, and laymen are vitally concerned with and interested in this great problem.

There can be little doubt that most general hospitals of fair size will eventually institute a program of routine admission examination of the chests of all hospital and clinic patients. There has been considerable hesitancy on the part of hospital administrators and roentgenologists as a whole to adopt such measures. The latter group can exert inestimable influence in the advocacy of such programs. It is of prime importance that hospital administrators coordinate their efforts in sponsoring such programs. The principles so comprehensively analyzed by Garland<sup>1</sup> are worthy of consideration by all parties concerned. Hospital chest screening assumes even greater importance as an instrument in the development of facilities and supervision which can eventually be utilized and enlisted in mass surveys of the population.

Chest screening of all hospital admissions does not pose many of the difficulties inherent in a general mass survey. There is little to add to Hodges'<sup>2</sup> comprehensive analysis of the problems and results of routine fluororoentgen chest examinations of all hospital admissions. Our findings coincide with his statistics gathered in a general hospital. We concur with his expression that chest examinations in general hospitals can be made workable and effective without overloading or hampering the department of roentgenology. To say the least, chest diagnosis becomes more

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fascinating and valuable, especially as a part of a teaching program of a general hospital. It is interesting to find, as Hodges<sup>2</sup> observes in his paper, that the detection of tuberculosis does not comprise the main purpose of hospital surveys. The discovery of other unsuspected lesions assumes at least equal importance. Pulmonary tuberculosis in Hodges' and our series of hospital admission examinations constitutes approximately 10 per cent of all the abnormal and pathologic findings of clinical importance.

While a survey project can become incorporated in the general routine of hospital procedures without serious obstacles there are many problems which are worthy of consideration and must be solved before the program can be expected to function properly and efficiently. The main prerequisite is a certified roentgenologist in attendance who can provide proper supervision and interpretation of the films. Twenty-four hour service sooner or later is essential if any reasonable degree of success is to be attained so far as the percentage of admissions examined is concerned. To further implement the successful operation of the project the x-ray equipment is preferably housed adjacent to the admitting room.

At the Evangelical Deaconess Hospital Milwaukee, Wisconsin, a plan to examine the chest of all hospital admissions was devised and approved in 1945 but the equipment did not arrive until 1947. At the inception of the program active and passive resistance was displayed by some of the members of the attending staff but this antagonism was soon abolished when the results of chest screening were divulged. All of the physicians now exhibit a lively interest in the program and the lesions uncovered. The chest films are interpreted the morning after admittance. The findings are always reported prior to scheduled surgery. In such manner a surgeon is often enabled to choose an optimum anesthetic agent under the prevailing cardiopulmonary conditions, thereby probably reducing morbidity and perhaps mortality to a minimum. In some instances operations are cancelled when the chest findings are disclosed. Many so-called early malignant lesions of the bowel, urinary tract, etc., when least suspected are not infrequently the cause of demonstrable metastatic lesions to the chest, as has been our experience in this work. There can be little doubt that the routine chest screening of hospital admissions is destined to assume equal, if not greater, status and importance than other routine laboratory analyses. Hodges<sup>2</sup> contends, and rightly so, that routine chest examinations of hospital and clinic patients will reveal more positive findings than serologic testing for syphilis, similarly applied.

We shall not delve into a detailed discussion of the advantages

and disadvantages of the various methods of chest screening. The problems vary in different institutions and communities. We have found the 4 x 5 inch stereo fluororöntgen film most suitable for our purposes. De Lorimer<sup>3</sup> analyzes the various methods of examination of the chest according to terms of trust for single case study, trust for mass studies, coordination with other examinations, future reference, unit cost per examination, and initial cost of equipment. His analysis led to official adoption of the stereoscopic technic with the 4 x 5 inch film for the United States Army.

Birkelo and his colleagues<sup>4</sup> present the results of a detailed investigation of the various methods of chest screening so far as effectiveness in tuberculosis case finding is concerned. They find that purely from the standpoint of effectiveness of tuberculosis case finding none of the methods, not even the 14 x 17 inch celluloid, is superior to the others. We favor, therefore, for purposes of a more general appraisal of the thoracic structures, the largest of the miniature films, so to speak, the 4 x 5 inch stereo. This method seems capable also of providing a fairly accurate evaluation of cardiac size when correction for distortion is made. Levitt<sup>5</sup> in his report of 10,000 chest examinations with stereoscopic fluororöntgen equipment finds the 4 x 5 inch stereo film most satisfactory for chest survey, more economical than the 14 x 17 inch film, and having the same, if not better, diagnostic accuracy.

The interpretation of survey films is wrought with some danger. Birkelo and his associates<sup>4</sup> show that there are many inter- and intra-individual variations. They justly conclude that in mass surveys films should be read by at least two interpreters. At the Deaconess Hospital at least two and sometimes three examiners interpret the films independently. Not infrequently one or the other is found guilty of over- and underreading—paralleling the findings of Birkelo and his colleagues. If such interpretative ser-

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TABLE 1

Number of Admissions July 1, 1947 to March 15, 1948	4655
Number of fluororöntgen examinations of chest	3626
Percentage of admissions examined	77.8
No fluororöntgen examinations	
Large chest film requested on admission	
Chest film within six months prior to admission	
Readmission—less than six month interval	
Physical condition not permitting coronary thrombosis, fracture cases, head injuries, cerebral accidents, etc	
Patients refusing examination	
Patients entering or leaving hospital when x-ray department closed	

vices are not available it seems desirable for the roentgenologist to review the films at least once

From July 1, 1947 to March 15, 1948, 3,626 fluororoentgen chest examinations have been performed at the Evangelical Deaconess Hospital, Milwaukee, Wisconsin. This number represents 77.8 per cent (Table I) of all hospital admissions during the same period. During the past few months our efficiency in this respect is greater, 80-85 per cent of all admissions are examined but it seems unlikely that this figure can be improved without 24 hour technical services

TABLE 2

Number of examinations July 1, 1947 to March 15, 1948	3626
	<i>Per cent Cases</i>
Essentially negative findings	71.4 2591
Abnormal findings of little or no clinical significance	18.4 667
Abnormal and pathologic findings warranting further study by 14 x 17 inch films, etc	9.4 342
Pathologic findings diagnosis certain and no further studies necessary	8 26

TABLE 3

## Abnormal and Pathologic Findings

	<i>Cases</i>	<i>Per cent</i>
Heart, abnormal contour and/or enlargement	171	4.7
Aortic abnormalities dilatation, tortuosity, arteriosclerosis, apparent absence	124	3.4
Superior mediastinal widening substernal thyroid dilatation innominate artery, enlarged thymus	55	1.5
Pleural thickening	119	3.3
Pleural effusion	8	.2
Diaphragm elevation, wavy, flattened	110	3.0
Rib abnormalities, metastasis, cervical, ect	82	2.0
Scoliosis	85	2.0
Probably tuberculosis	46	1.25
Probably active — 3		
Probably inactive — 43		
Pulmonary pathology, undetermined origin (Bronchiectasis, chronic pneumonitis, etc)	39	1.00
Increased markings	123	3.3
Pneumoconiosis	2	.05
Emphysema	176	4.8
Metastasis, suggestive and definite	18	.5
Atelectasis, plate-like (Fleischner lines)	4	.1
Hilar enlargement	27	.75

Approximately 71.4 per cent of the total number examined were interpreted as essentially negative (Table 2). In 18.4 per cent abnormal findings were discovered but these findings were assumed to be of little or no clinical significance. Over 10 per cent of the patients examined showed abnormalities obviously of pathologic significance and clinical interest.

Almost 5 per cent of all patients examined showed abnormal cardiac contours and/or evidence of enlargement. Of these a good number were cases of prominence of the pulmonary conus in pregnant women. We find that many of the pregnant women registering at the hospital 6-8 weeks before expected delivery exhibit such pulmonary conus enlargement. It is interesting to relate that in two such patients pulmonary changes were described on registration but the warnings were unheeded. A few to several weeks later these same patients were admitted to the hospital with toxemias of pregnancy—pre-eclamptic. In our series of 3,626 chest examinations 46 patients, representing an incidence of approximately 1.25 per cent, showed changes consistent with or due to tuberculosis, some “unstable,” 3 probably active. Two cases of pneumoconiosis are also listed. Metastatic lesions in the chest constituted an important group, most of which were unsuspected. Eighteen such cases were discovered. The management of these cases was altered in most instances. To our surprise at least 27 patients (0.75 per cent) displayed suggestive and definite hilar node enlargement, bilateral in many instances. Follow-up studies of such patients is imperative.

Chest screening is valuable in still another respect. The fluororöntgen study of the chest on admission provides a “control” film. Should occasion arise for subsequent chest studies, post-operatively or otherwise, comparison of the films provides an excellent basis for interpretation. Whereas previously equivocal findings or slight apparent deviations from the “normal” were discounted or at best considered indication for later studies, now any slight change or new development in the chest receives its due consideration, often permitting of more precise diagnostic statements and earlier diagnosis. Suitable treatment can thus be instituted at an earlier stage of the complication, thereby reducing morbidity.

Landau and Schorsch<sup>6</sup> state that from 8 to 22 per cent of all general hospital and clinic patients show disease in routine chest films. This percentage of positive findings is indeed higher than with any of the other accepted routine laboratory procedures.

In 1934 Hodges<sup>7</sup> made a test of the utility of routine x-ray surveying of all patients' chests during 14 consecutive working days. They developed the films, put them away for three months, and

at the end of this period interpreted the films. They delved into the hospital records of the patients to see whether or not the examination might have been helpful in the diagnosis. They found that as a group they had made a gross error of omission once every day during that 14 day period. They felt that the medical profession could not afford an error of that extent, if it could be avoided. Thus, admission chest films in many instances obviate unnecessary floundering with diagnostic methods. In this period of hospital bed shortages any acceleration of our diagnostic services in effect provides more available hospital days.

### SUMMARY AND CONCLUSIONS

The routine chest screening of hospital admissions by the fluororoentgen method is practicable in most general hospitals where the x-ray department is directed by a certified roentgenologist. Such procedures yield results of at least equal, if not greater, magnitude than other routine hospital laboratory procedures.

Abnormal and pathologic conditions of the chest of clinical importance are discovered in approximately 10 per cent of chests examined in hospital screening programs. About 10 per cent of these pathologic findings are probably due to pulmonary tuberculosis. Although pulmonary tuberculosis represents a relatively small percentage of the clinically important findings, such case detection in hospitals is extremely important for several reasons: (1) It minimizes exposure of other hospital patients to tuberculosis by providing reason for segregation or transfer. (2) It permits of early diagnosis and institution of proper therapy. (3) It minimizes exposure of hospital personnel to tuberculosis. (4) It provides valuable data in compensation matters and disputes.

Nontuberculous diseases of the chest in hospital surveys are of much greater frequency and probably of equal importance. Cardiac abnormalities, mediastinal tumors or widening, enlarged hilar nodes, metastatic lesions, etc., account for approximately 90 per cent of the pathologic conditions uncovered by this method.

Admission chest fluororoentgenograms provide at least one more advantage. The availability of so-called "control" films of the chest is of great value in those instances where chest complications develop during the hospital stay or even at a later date after discharge from the hospital. Comparison of the "control" films with subsequent roentgen studies affords criteria which often permit of unequivocal diagnostic statements. With such comparative roentgen studies of the chest, diagnostic uncertainty is often reduced to a minimum.

The viewpoint of the roentgenologists as regards chest surveys or screening is no different from the viewpoint of the medical



profession in general, that is, to provide feasible, well planned and supervised programs. Such planning is mandatory if the procedure is not to be discredited and the reputation of the medical profession is to be sustained. It is imperative that the medical profession undertake and supervise such programs if leadership in public health matters is to be regained and retained.

### RESUMEN Y CONCLUSIONES

El examen sistemático del pecho de las admisiones a los hospitales mediante el método fotoroentgenográfico es aplicable a la mayoría de los hospitales generales donde el departamento radiológico está dirigido por un roentgenólogo certificado. Tales procedimientos dan resultados por lo menos iguales, si no de mayor magnitud que cualquier otro procedimiento sistemático de laboratorio del hospital.

Se descubren estados anormales y patológicos del torax de importancia clínica en aproximadamente el 10 por ciento de los pechos examinados en esos programas de exámenes en los hospitales. Un 10 por ciento de esos hallazgos patológicos se deben probablemente a la tuberculosis pulmonar. Aunque la tuberculosis pulmonar representa un porcentaje relativamente pequeño de los hallazgos de importancia clínica, el descubrimiento de esos casos en los hospitales es extremadamente importante por varias razones: (1) Reduce al mínimo la exposición de otros pacientes del hospital a la tuberculosis, pues suministra una razón para el aislamiento o la transferencia. (2) Permite el diagnóstico temprano y la aplicación de la terapia apropiada. (3) Reduce al mínimo la exposición del personal del hospital a la tuberculosis. (4) Suministra datos valiosos en cuestiones y disputas de indemnización.

En los censos de hospital las enfermedades torácicas no tuberculosas son de mucha mayor frecuencia y probablemente de igual importancia. Las anomalías cardíacas, los tumores o el ensanchamiento del mediastino, los ganglios hiliares hipertrofiados, las lesiones metastásicas, etc., representan aproximadamente el 90 por ciento de los estados patológicos que se descubren por este medio.

Los fotoroentgenogramas torácicos tomados durante la admisión tienen por lo menos una ventaja adicional. La disponibilidad de las llamadas películas torácicas "de control" es de gran valor en esos casos en los que ocurren complicaciones torácicas durante la estancia en el hospital o aun después de haber sido dados de alta del hospital. La comparación de las películas "de control" con estudios roentgenológicos subsiguientes suministra criterios que a menudo permiten declaraciones diagnósticas inequívocas.

Con tales estudios roentgenologicos toracicos comparativos, frecuentemente se puede reducir al minimo la incertidumbre del diagnóstico

El punto de vista de los roentgenólogos acerca de los censos radiograficos toracicos no difiere del punto de vista de la profesión medica en general, es decir, de proveer programas factibles, bien ideados y supervisados. Es obligatorio hacer esos planes si se desea evitar que se desacredite el procedimiento y se quiere sustentar la reputación de la profesión médica. Es imperativo que la profesión medica lleve a cabo y supervise tales programas para que pueda recobrar y retener la dirección de las cuestiones de sanidad publica

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# The Combined Use of Streptomycin and Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis\*

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## *Introduction*

In this paper the authors are attempting to evaluate a combined mode of therapy for the treatment of pulmonary tuberculosis consisting of pneumoperitoneum and streptomycin. No attempt is being made to compare these two methods of treatment, but to see if a combination of the two is not the best means of therapy in certain types of cases. It has been our experience at Fitzsimons General Hospital that a number of cases of pulmonary tuberculosis with cavitation treated with streptomycin have shown good results during the course of treatment but a reappearance of cavitation upon the discontinuation of streptomycin. This has also been the experience of Hinshaw, Feldman and Pfuetze,<sup>2</sup> the cooperative study of Army, Navy, Veterans Administration,<sup>5</sup> and Canada.<sup>6</sup> D'Esopo and Steinhaus<sup>12</sup> also emphasize that relapses occur in a significant number of cases toward the end of treatment as well as shortly afterwards and felt "that there might be an optimum time during the course of therapy when the institution of collapse procedures might have preserved what improvement had occurred."

It has been our experience at Fitzsimons General Hospital that usually these cases with reopened cavities become positive for tubercle bacilli again and that in 70-80 per cent the organism is resistant to streptomycin in 100 micrograms per cubic centimeter. As shown by Fisher and his associates<sup>7</sup> this has occurred whether the dosage is 1.8 or 10 grams (Fisher<sup>14</sup>). Consequently we have been attempting to follow the successful or incomplete closure of cavities during streptomycin therapy with some type of temporary collapse measure. In this paper we are discussing the cases treated only with one type of collapse measure, namely pneumoperitoneum, and we hope to present pneumothorax used in conjunction with streptomycin in a later paper.

The indications for the type of temporary collapse measure selected are the same as cases untreated by streptomycin. In this

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series of cases pneumoperitoneum was used especially in cases with cavities notoriously difficult to close with other collapse measures, such as basilar and hilar cavities (Rafferty<sup>17</sup>) In addition the usual indications for pneumoperitoneum were used (Banyai<sup>15</sup>) Our primary criteria for the use of pneumoperitoneum were

- A) Pneumothorax unsuccessful or contraindicated
- B) Bilateral cavitory disease
- C) Diseases unsuitable for thoracoplasty
- D) Preparative for surgical procedures

The authors are of the opinion that pneumoperitoneum should not be considered as a last ditch measure, or following the exclusion of all other collapse measures, but rather as a definitive measure in itself (Editorial,<sup>18</sup> "Diseases of Chest")

Crow and Whelchel<sup>16</sup> reported a series of 546 cases of pneumoperitoneum with diaphragmatic paralysis in which 63 per cent showed apparent closure of all cavities Sixty-four per cent of these cases had far advanced disease We will attempt to show in this paper that good results can be obtained by the use of adequate pneumoperitoneum in conjunction with streptomycin therapy

### *Criteria for the Selection of Cases*

This series is composed mainly of young white males on active duty in the armed forces or recently discharged In addition it includes 2 females and several older males In all cases sputum cultures were positive for *Mycobacterium tuberculosis*, and all cases were being actively treated with pneumoperitoneum at Fitzsimons General Hospital at the time of this study Cases are usually kept at Fitzsimons General Hospital for only a relatively short period of time before being sent to a Veterans Hospital so that the length of time these cases were observed was by necessity limited It was found that the average was approximately six months time and it should be emphasized that this is a short term study of the benefits of this combination of treatment All of these patients were maintained on absolute bed rest or bed rest with lavatory privileges

### *Technique*

Streptomycin was administered in the following schedule of doses

- 14 received 1 Gm/day divided into 2 daily doses for 45-60 days
- 6 received 1 Gm/day divided into 2 daily doses for 90-120 days
- 2 received 2 Gm/day divided into 5 daily doses for 60 days
- 7 received 2 Gm/day divided into 5 daily doses for 120 days
- 1 received 2 Gm/day every third day for 120 days

7 received 2 Gm/day for 60 days decreased to 1 Gm/day another 60 days  
4 received additional treatment with aerosol for 6-16 weeks

The cooperative study by Army, Navy, Veterans Administration<sup>5</sup> has shown that 1 gm of streptomycin daily appeared to be quite as effective in pulmonary tuberculosis as the regimen of larger doses. In 1 case streptomycin was discontinued because of severe vertigo. Aerosol administration of streptomycin is not being used at this hospital any longer because of frequent sensitization of patients as well as nursing personnel that occurs during nebulization. Similar if not superior results to nebulization can be obtained by injection.<sup>5</sup>

Adequate pneumoperitoneum of the type recommended by Brock<sup>19</sup> consisting of refills of at least 1000 cc of air weekly, and frequently semi-weekly, was used. In 18 cases this was aided by a phrenemphraxis of the more involved side in bilateral disease and the affected side in unilateral disease. In 1 case pneumothorax was an additional concurrent procedure. No abdominal supports were used. In a few cases insulin was given to promote appetite.

Monthly x-ray films, weight, sputum cultures and smears, and sedimentation rates were taken. Gastric washing cultures were obtained in those patients who did not have sputum or whose sputum was negative on smear or culture. Streptomycin sensitivity tests were performed on all cultures positive for tubercle bacilli after treatment with streptomycin. Apical, Bucky and laminogram x-ray films were taken as circumstances required.

### *Results*

Fifty seven patients who have received treatment with pneumoperitoneum for pulmonary tuberculosis at Fitzsimons General Hospital during the year 1947-48 constitute this series. Of this group 37 cases received, in addition to pneumoperitoneum, a course of streptomycin therapy. The majority of these cases were observed for an average of six months time, the longest being 1½ years, the shortest being 2 months. Most of the cases were under treatment for far advanced pulmonary tuberculosis.

In the cases treated by pneumoperitoneum alone either there was no streptomycin available or the protocol for treatment did not include these cases at that time. As streptomycin became more available the frequency of its use as an adjunct to pneumoperitoneum in the treatment of far advanced pulmonary tuberculosis increased considerably. Consequently, only a few cases have been treated by pneumoperitoneum alone during the past 6 months.

Streptomycin in the treatment of far advanced tuberculosis was shown to be definitely beneficial by Hinshaw, Feldman and Pfuetze.<sup>2</sup>

*Streptomycin in Conjunction with Pneumoperitoneum*

Thirty-seven cases of pulmonary tuberculosis were treated with a combination of streptomycin and pneumoperitoneum. Of these 27 (73 per cent) were far advanced cases and 10 (27 per cent) were moderately advanced. There were no minimal cases in this series. Rapid spontaneous regression was not likely to occur in that most of the patients had been on routine bed rest for several months and had not improved. All patients had moderate to severe constitutional symptoms (Table I).

Of the 37 cases 20 were cases in which streptomycin was started at least 1 month prior to pneumoperitoneum, 8 in which pneumoperitoneum preceded streptomycin by at least 1 month, and 9 where both were instituted at approximately the same time.

In this group of cases, evidence that pulmonary cavities had closed was observed in 21 patients, cavitation persisted in 16 cases. Definite roentgenologic improvement was considered from very good to excellent in 21. Little or no roentgenologically demonstrable improvement was seen in 5 cases. Tubercle bacilli disappeared from the sputum in 24 cases. This was substantiated by sputum smears and cultures and gastric washing cultures. Sputum was not converted in 7 patients in spite of at least 6 months treatment (See Table II). An additional 6 under observation for less than 6 months remained positive. In no cases under treatment was progression of the disease observed. In 1 case the patient continued to show roentgenologic improvement although the *Mycobacterium tuberculosis* was found to be resistant to streptomycin. None of the patients in this series died.

Clinical improvement as evidenced by significant improvements in sedimentation rate, weight, sputum production, cough, increased appetite, and generalized well being was excellent in 20 cases or

TABLE I  
Pneumoperitoneum in Conjunction with Streptomycin

	SEX		COLOR			
	M	F	White	Negro	Others	
Number	34	3	29	5	3	
Per cent	92	8	79	13	8	

	AGE				CLASSIFICATION			SPUTUM BEFORE TREATMENT	
	Teen	20-29	30-39	40-50	Min	Mod Adv	Far Adv	Pos	Neg
Number	6	17	10	4	0	10	27	37	0
Per cent	16	46	27	11	0	27	73	100	0

54 per cent and good in 12 cases or 33 per cent. This was one of the most striking features of this study.

Of the 20 cases in which streptomycin was followed by pneumoperitoneum, it was found that 15 obtained no cavity closure on streptomycin alone but that in those cases in which pneumoperitoneum was induced within 2 months following the course of streptomycin, the following results were obtained:

- 1 closed cavity 0-1 month after pneumoperitoneum induced
- 7 closed cavity 1-2 months after pneumoperitoneum induced
- 1 closed cavity 2-3 months after pneumoperitoneum induced

**TABLE II**  
Clinical Summary of 37 Cases Treated with Streptomycin  
and Pneumoperitoneum

	Streptomycin followed by Pneumoperitoneum	Pneumoperitoneum followed by Streptomycin	Started Together	Total	Per cent
Number of cases	20	8	9	37	100
Sputum converted	13	3	8	24	65
Sputum not converted	7	5	1	13	35
Cavities					
Closed	13	2	5	20	56
Smaller	5	2	2	9	24
Unchanged or Worse	2	4	1	7	19
Roentgenologic Improvement					
Excellent	12	3	6	21	57
Good	7	1	3	11	30
Slight	1	1	0	2	5
None or worse	0	3	0	3	8
Clinical Improvement *					
Excellent	12	2	6	20	54
Good	7	2	3	12	33
Moderate	1	2	0	3	7
Slight	0	1	0	1	3
Unchanged or worse	0	1	0	1	3

\*Sedimentation rate, weight, sputum production, fever, increased appetite, and cough

- 1 closed cavity 4-5 months after pneumoperitoneum induced
- 1 closed cavity over 6 months after pneumoperitoneum induced
- 4 obtained no cavity closure

In this group of 15 cases with no cavity closure, 10 showed complete cavity closure within 6 months of pneumoperitoneum treatment. Of the 4 cases that failed to close cavities, 2 had been on pneumoperitoneum for only one month at the time this paper was written.

In another group consisting of 4 patients with pneumoperitoneum from 2-6 months following streptomycin, 2 closed their cavities within 3 months of pneumoperitoneum treatment and 2 have failed to do so.

The last of these 20 cases closed his cavity on streptomycin alone after 3-4 months treatment. The pneumoperitoneum was induced in this patient before the streptomycin was discontinued to maintain cavity closure. It is felt that this has been accomplished.

Nine patients were treated with streptomycin and pneumoperitoneum started simultaneously. This group showed the most favorable results. Five cases showed cavity closure on x-ray examination. One case had no cavities but had extensive disease. Three cases showed no definite cavity closure on the x-ray film. In two of these cases the presence of cavitation was equivocal, but since there has been some doubt, they were included as incomplete.

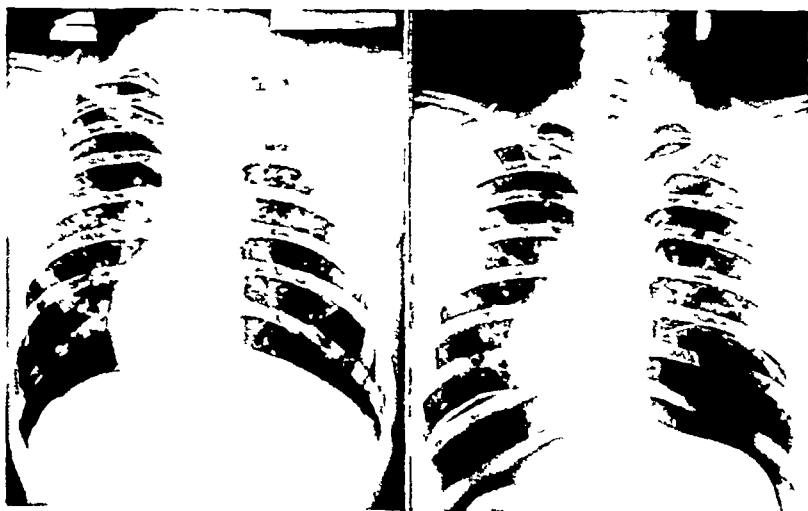


FIGURE 1

FIGURE 2

*Figure 1 Case 1* X-ray film No 1 taken March 18 1947 before pneumoperitoneum or streptomycin started—*Figure 2 Case 1* X-ray film No 2 taken July 29 1947 showing marked clearing bilaterally. No evidence of cavitation. Patient had been on combined treatment of pneumoperitoneum and streptomycin for approximately two months.





FIGURE 1

FIGURE 2

FIGURE 3

Figure 1, Case II X-ray film No 1, taken November 7, 1947, before pneumoperitoneum or streptomycin started—Figure 2, Case II X-ray film No 2, taken January 27, 1948, after six weeks of treatment with streptomycin Residual cavitation remaining in left upper lobe Streptomycin was discontinued at the time this film was taken—Figure 3, Case II X-ray film No 3, taken February 24, 1948, after one month of pneumoperitoneum, showing further regression of infiltration in left upper lobe No evidence of cavitation

cavity closure. However, both of these cases have been negative in sputum examinations for several months.

The third group of 8 patients under observation was treated by pneumoperitoneum and was followed in 1-12 months by streptomycin therapy. This group showed the poorest results. Four patients showed no cavity closure on streptomycin, but 1 patient closed his cavity 2-3 months following a course of streptomycin while on pneumoperitoneum. Of the remaining 4 patients, 2 showed cavity closure within 4-5 months following streptomycin while on pneumoperitoneum. The poor results of this group may be explained on the basis of the long duration of far advanced disease from which all of these patients suffered. This group demonstrates the advisability of using streptomycin early in the course of the disease, if good results are to be expected.

It is felt that the following case is a rather typical one and shows the excellent results that can be expected by this combined treatment. Another x-ray illustration is shown, but the case is not being presented for the sake of brevity.

*Case 1* This 21 year old white male was admitted to Fitzsimons General Hospital on April 2, 1947 with a history of the onset of his disease in February 1947, with severe constitutional symptoms. He had a cough productive of  $\frac{3}{4}$  cup of sputum positive on smear and culture for tubercle bacilli. Temperature was 100 degrees F. Sedimentation rate was 29 mm/hr (Wintrobe). X-ray film on admission revealed an exudative area of infiltration in the right upper lobe with two cavities measuring  $2 \times 2.5$  cm, one in the 1st interspace and the other under the 2nd anterior rib. Exudative-caseous disease involved all lobes of the left lung, but was most extensive in the 2nd, 3rd and 4th interspaces. A cavity  $2.5 \times 3$  cm was present in the 2nd interspace on the left (See Fig. 1). A right pneumothorax was attempted on April 9, 1947 but was unsuccessful. On April 25, 1947 streptomycin (2 gm/day, divided into 5 doses) was started. On May 16 a pneumoperitoneum was induced and on May 31, 1947 a right phrenemphraxis was added. Streptomycin was discontinued on August 25, 1947.

Temperature became normal 3 weeks after streptomycin was started and in July 1947 sedimentation rate was normal. There was a marked improvement in the cough at this time and he produced only 4-15 cc sputum in 24 hours. Sputum has been negative on smear and culture since July 1947.

X-ray film taken at the conclusion of streptomycin therapy showed remarkable clearing with no definite evidence of cavitation visible. A substantial pneumoperitoneum was present. He continued to show clearing on x-ray examinations even though the streptomycin was discontinued, and by January 1948 there were only a few fibrous strands visible.

Twenty cases were treated by pneumoperitoneum alone (See Tables III and IV). Fourteen cases were treated for less than 6 months. Five of these cases obtained cavity closure as seen on x-ray films and in 7 additional cases there was significant de-

crease in cavity size Thirteen of these cases had a positive sputum before treatment and 8 have obtained sputum conversion

Six cases were treated for more than 6 months Of these 2 obtained cavity closure and 2 had significant decrease in cavity size Two cases had sputum conversion with all six being positive originally

### Discussion

It is important to realize that we are not attempting to compare pneumoperitoneum alone with a combined method of pneumoperitoneum and streptomycin The only reason we included those cases treated by pneumoperitoneum alone was to demonstrate the type of results that are obtained at Fitzsimons Hospital when only

TABLE III  
Pneumoperitoneum Alone

	TOTAL CASES	S E X		C O L O R	
		Male	Female	White	Negro
Number	20	19	1	16	4
Per cent	100	95	5	80	20

	A G E				CLASSIFICATION		
	Teen	20-29	30-39	40-49	Min	Mod Adv	Far Adv
Number	0	12	7	1	0	8	12
Per cent	0	60	35	5	0	40	60

TABLE IV  
Pneumoperitoneum Only Treatment

	Total No of Cases	Cavity Closure	Cavities Significantly Decreased In Size	Unchanged	Sputum Conversion	Negative Before Treatment	Positive Before Treatment
Under 6 Mos	14	5	7	2	8	1	13
Over 6 Mos	6	2	2	2	2	0	6

	Improvement X-Ray	Improvement* Clinical
Excellent	7	5
Moderate	6	9
Slight	5	3
Unchanged or worse	2	3

\*Sedimentation rate, weight, sputum production, fever, increased appetite, and cough

pneumoperitoneum is used. Cavity closure was obtained by only one-third of the cases we presented where streptomycin was not used. We realize that this is only a short term observation and that some of these cases might later show cavity closure. When streptomycin was used, cavity closure rate was almost doubled, with 57 per cent obtaining closure and 65 per cent sputum conversion. In addition 87 per cent of our cases showed either good or excellent x-ray evidence of regression of lesions when treated with combined therapy. We feel that this is of significance.

In the group of cases treated by pneumoperitoneum unsuccessfully and followed by a course of treatment of streptomycin, less satisfactory results were obtained. This may be explained by the interval elapsing between the onset of disease and institution of therapy. The authors are of the opinion that this series indicates that better results can be obtained if early combined treatment is instituted, in view of the results presented in tables I and II.

We feel that this paper is a further tribute to the value of streptomycin in the treatment of pulmonary tuberculosis, but that the startling results in many of these cases were not due to streptomycin alone. This is best shown by the group of 15 cases that did not show cavity closure on streptomycin but in which 10 showed complete cavity closure within 6 months post-streptomycin while on pneumoperitoneum. In addition there was one case whose cavity closed during the 3rd month of streptomycin therapy and in which we believe that pneumoperitoneum was instrumental in maintaining cavity closure. These findings are in line with the data presented by D'Esopo and Steinhaus<sup>12</sup> in which they conclude that "The infrequency of cavity closure suggested the use of streptomycin as an adjunct to collapse procedures."

Good results were obtained in two of our methods of treatment, namely, (a) streptomycin followed by pneumoperitoneum, (b) streptomycin and pneumoperitoneum introduced simultaneously. Although pulmonary physiology studies reveal a decreased circulation to a partially relaxed lung which in turn might mean a lessened amount of streptomycin brought to the diseased tissue, this was not apparently significant in view of the good results that were obtained in our series. It remains for future observation to determine the optimal time for the introduction of pneumoperitoneum or other collapse measures in relation to streptomycin. We think that the trend of therapy in pulmonary tuberculosis will be toward early collapse of cavitory lesions accompanied by a course of streptomycin at approximately the time the collapse measure is instituted. This may save the patient months if not years of hospitalization.

Five cases with extensive bilateral cavitory disease were made

ready for surgical procedures, such as thoracoplasty or extra-pleural pneumonolysis with lucite balls. This surgery may eventually result in cure of their disease. The probable ultimate salvage of these cases is rather encouraging in view of the hopeless outlook for these patients when they were first hospitalized and started on the pneumoperitoneum-streptomycin treatment.

### SUMMARY

1) This is a series of 57 cases of pulmonary tuberculosis in predominately young white males treated at Fitzsimons General Hospital during 1947-1948.

2) Thirty nine far advanced cases and 18 moderately advanced cases were observed. No minimal cases are included in this series.

3) Thirty seven cases were treated with a combined program of streptomycin plus pneumoperitoneum.

4) This group was subdivided into

(a) Twenty cases treated with streptomycin followed by pneumoperitoneum.

(b) Eight cases treated with pneumoperitoneum followed by streptomycin.

(c) Nine cases treated with streptomycin plus pneumoperitoneum started simultaneously.

5) In group (a) 13 had sputum conversion and 13 had cavity closure. In group (b) 3 had sputum conversion and 2 had cavity closure. In group (c) 8 had sputum conversion and 6 had cavity closure.

6) Twenty cases were treated with pneumoperitoneum alone and are included to demonstrate the type of result to be expected by this treatment.

7) The results seem to indicate that the best treatment for far advanced and moderately advanced cases, not suited for major surgery and in whom pneumothorax is not indicated, is the combined use of streptomycin and pneumoperitoneum as early in the course of the disease as possible.

### RESUMEN

1) Se presenta una serie de 57 casos de tuberculosis pulmonar en hombres predominantemente jóvenes y blancos, tratados en el Hospital General Fitzsimmons durante el período de 1947 a 1948.

2) Se observó a 39 casos muy avanzados y 18 moderadamente avanzados. No se incluyen casos mínimos en esta serie de casos.

3) Se trató a 37 casos con un programa combinado de estreptomicina y neumoperitoneo.

4) Se subdividió a este grupo en

(a) Veinte casos tratados con estreptomicina seguida de neumoperitoneo.

(b) Ocho casos tratados con neumoperitoneo seguido de estreptomycin

(c) Nueve casos tratados con estreptomycin y neumoperitoneo comenzados simultáneamente

5) En el grupo (a) en 13 se convirtió el esputo y en 13 se cerraron cavernas En el grupo (b) en 3 se convirtió el esputo y en 2 se cerraron cavernas En el grupo (c) en 8 se convirtió el esputo y en 6 se cerraron cavernas

6) Se trató a 20 casos con neumoperitoneo solo y se los incluye para demostrar la clase de resultado que se puede esperar con este tratamiento

7) Los resultados parecen indicar que el mejor tratamiento para casos muy avanzados y moderadamente avanzados, no adaptables para la cirugía mayor y en los que no está indicado el neumotórax, es el uso combinado de la estreptomycin y el neumoperitoneo tan temprano en la evolución de la enfermedad como lo sea posible

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# Propagating Pulmonary Artery Thrombosis\*

## (A Specific Syndrome\*)

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In considering pulmonary vascular occlusion, one often neglects propagating thrombi of the main stem and right or left branches of the pulmonary artery. The attention is usually centered upon pulmonary embolism which results in infarction or sudden death. There is, however, a specific syndrome that is produced by thrombosis of the pulmonary trunk or its right and left branches. The thrombus by propagation gradually reduces blood flow through the pulmonary arterial tree and concomitantly resists outflow from the right ventricle. For purposes of clarity, the pulmonary arterial tree is divided into (a) the pulmonary trunk and its two branches, (b) the lobar divisions, and (c) the lobular arteries. Thrombosis occurs most commonly at site (c) (lobular branches) as the result of vascular obliteration by pulmonary disease. Rarely thrombosis occurs in position (b) (lobar branches) and may cause infarction or death. This discussion is concerned with progressively propagating thrombi at site (a) (pulmonary trunk and its two main branches) and the resultant specific syndrome which develops secondary to the blockage of blood flow through the entire lung.

The condition was first reported by Heile in 1837<sup>1</sup> and as early as 1897 Dickinson<sup>2</sup> was aware that the condition occurs even in young children. However, by 1934, only 26 cases had been reported in the literature.<sup>1</sup> In recent years many additional cases have been recognized and reported. The standard medical texts merely imply that pulmonary artery thrombosis is rare, but Harvey and Hogg<sup>3</sup> stated that the incidence falls between 0.9 per cent and 0.7 per cent when computed on the basis of necropsy reports. It is well recognized that even though the condition has occurred in a two year old child it is much more common in individuals who have progressed beyond middle life. Middleton,<sup>4</sup> who bases his statements on 53 necropsy cases, feels that the situation develops more frequently in men than in women. He gives a ratio of 3.4 to 1.

Roughly one-half of the cases have an acute onset and the remaining one-half develop slowly. Actually the duration has

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ranged from a few minutes to that of one or more years. Of the cases that the author reviewed, the longest in duration was one and one-half years<sup>5</sup> but it was not uncommon for the patient to remain alive for a four week period. About 10 per cent of the cases die in the first 12 hours and the remainder may live 10 days or more.<sup>4</sup>

The clinical symptoms show variation but nearly all of the cases regardless of etiology, will show dyspnea. In the cases reported by Middleton, 90 per cent had dyspnea, 50 per cent had hemoptysis, 50 per cent had cyanosis, 25 per cent had cough, 25 per cent had pain in the chest or in the epigastrium, 25 per cent were apprehensive, and 20 per cent developed shock. Pou and Charr<sup>6</sup> in arranging the symptoms in order of frequency composed the following: dyspnea, cyanosis, engorged cervical vessels, pain in the chest or in the epigastrium, restlessness and mental confusion, exophthalmos and blurred vision, right heart failure with terminal edema. It is apparent that there are discrepancies between the two lists and actually many of the other cases reported failed to have some of the symptoms or had additional ones.<sup>16</sup> Thus, while it is admitted that considerable variations exist, the constant finding is that of dyspnea and most of the cases have cyanosis and others may have any of the above listed symptoms. If the onset is acute the patient is more apt to have dyspnea, cyanosis, chest pain, vomiting and signs of acute collapse, but if the condition develops gradually he will complain of dyspnea, cyanosis, cough and hemoptysis.

The dyspnea is extremely severe, out of proportion to that seen in cardiac failure and the cyanosis is so intense that it has been related to the cyanosis seen in Ayerza's disease.<sup>6</sup> The cyanosis begins in the head, particularly in the lips, nose and ears, and then involves the upper extremities causing bluish discoloration of the nailbeds. These conditions result from the reduction in the amount of blood that reaches the lungs.

As stated before, the pain may or may not be present and when it does occur it will not necessarily herald the difficulty but usually follows the dyspnea and cyanosis. Variation in the location of pain exists in that it may be beneath the sternum or in the epigastrium but it does not radiate. Finally, it may be excruciating or it may be a dull ache. A theoretical explanation for the abdominal pain is that it occurs as a result of an abnormal vagus reflex.<sup>4</sup> Restlessness and mental confusion, the results of anoxemia, occur uncommonly.

Considerable confusion exists concerning the character of the pulse pressure. It is reported to range from normal to very low. It can be said that the pulse pressure and the systolic pressure



are not affected to any marked degree in most cases Hemoptysis results from congestion of the pulmonary vascular bed as a result of anastomosis between the pulmonary vessels and the bronchial arteries in an attempt to circumvent the block <sup>17</sup> When the patient expires quickly, the engorged cervical veins and terminal edema which are manifestations of right heart failure do not develop However, eliminating accessory causes for death, the chronic cases will die with right heart failure

The thrombus causing this syndrome begins at the distal end of the right and left branches of the pulmonary artery and propagates retrogradely to the main bifurcation of the vessel but it may begin at the same site and propagate in the direction of the lung About four-fifths of the lumen may be obstructed In one-half of the cases the thrombus will ultimately end in bilateral involvement Savacool and Charr<sup>18</sup> feel that in the great majority of cases the thrombus begins in the right artery They were able to find only six cases of left pulmonary thrombosis However, other investigators feel that the site of origin is equally divided between the right and left branches of the pulmonary artery <sup>4</sup> This discrepancy may exist because all of the opinions concerning the site of origin are based on an attempt to tell the age of a particular part of the thrombus by its microscopic appearance In chronic cases the thrombus often shows organization but this does not necessarily indicate its oldest part

Many associated pathologic conditions are found in addition to the thrombus Fifty per cent of Savacool and Charr's cases were complicated by some type of pulmonary disease and in a great many of their cases pulmonary arteriosclerosis was found Other investigators feel that the outstanding associated pathologic lesions could be grouped under cardio-vascular disease with arteriosclerosis being the most important member of the group <sup>4</sup> If a list were to be prepared it would include mitral stenosis, tuberculosis, arteriosclerosis of the pulmonary artery, silicosis, bronchitis, lung abscess, myocardial degeneration, congenital heart disease, thrombophlebitis, coronary heart disease, and tumors of the mediastinum

Nearly all the chronic cases show hypertrophy and dilatation of the right ventricle and perhaps hypertrophy of the left ventricle as well

It is obvious from the above discussion that pulmonary artery thrombosis is a secondary complication of some pre-existing pathologic state and that the pathogenesis will vary depending upon the original disease Basically, while secondary factors may determine the site of formation of any thrombus, the condition is produced by either alteration of the vessel wall or disturbance in blood coagulation Consequently, chronic pulmonary disease will

predispose to the development of pulmonary artery thrombosis by two methods. First, the chronic disease by destroying the lung and capillary tissue ultimately increases the pulmonary arterial pressure and thus influences the development of arteriosclerosis<sup>19</sup> which in turn damages the vessel wall. Secondly, the chronic disease by causing obliterative endarteritis slows pulmonary circulation and thus influences the blood coagulation. Pou and Charr<sup>6</sup> feel that in their cases the thrombus always began in the vessel passing to the lung containing a lesion and in cases of bilateral pulmonary disease the thrombus began in the vessel passing to the more involved lung.

In cases associated with thrombophlebitis, it is thought that a pulmonary embolus develops and then a thrombus is superimposed upon the embolus. Over a period of time the thrombus builds up in a retrograde fashion and becomes organized.<sup>15</sup> Finally, the thrombus may develop secondarily to congenital heart disease, rheumatic fever, bacterial endocarditis, polycythemia, and tumor invasion of the pulmonary artery.

Experimentally in dogs the systemic pressure will not fall until 60 per cent occlusion occurs to the pulmonary artery and death does not intervene until roughly 90 per cent of the lumen is blocked.<sup>20</sup> These experimental data may explain the progressive syndrome in chronic cases having a gradual onset. In addition, the collateral circulation which is said to develop between the bronchial arteries and the pulmonary vessels<sup>17</sup> may compensate for a time, but when near complete blockage of the pulmonary artery occurs, the patient dies because blood enters the right heart but cannot leave it. However, if a patent septum exists, blood may pass from the right ventricle to the left ventricle, allowing the patient to live longer but he will show deep cyanosis.<sup>3</sup> At the necropsy table it has been frequently noted that the thrombus almost completely blocks the vessel and yet microscopic organization can be seen indicating that the pathologic alterations have existed for a considerable length of time.

Electrocardiographic tracings are not diagnostic but are of negative value. McGinn and White<sup>21</sup> found prominent Q waves in lead one and late inversion of the T wave with a high takeoff in lead three. Wade<sup>9</sup> had a case that showed slight depression of the S-T segments, and in the case reported from the Massachusetts General Hospital, such changes as right axis deviation, flat S-T segments, right bundle branch block and low voltage of the QRS complex were noted.<sup>13</sup>

Fluoroscopy and chest roentgenograms are of more value, in that these patients show a prominence of the pulmonary conus and of the pulmonary artery.

Cardioangiography is in its infancy, and although the author knows of no reported cases of pulmonary artery thrombus in which the procedure was employed, in his opinion such a method should materially aid in the diagnosis, particularly in chronic cases. The pulmonary conus and the pulmonary artery with its branches have been completely and clearly demonstrated by several investigators working with cardioangiography and any block should be detected readily.

The differential diagnosis of congenital heart disease is of particular importance in children and young adults. Usually the patients with congenital heart disease have a history of a very prolonged illness, but in the opinion of Harvey and Hogg<sup>3</sup> if a sudden increase in the severity of the symptoms should occur, one must suspect superimposed thrombosis of the pulmonary artery.

In pulmonary embolism, the cyanosis and substernal or epigastric pain are not as severe as is seen in pulmonary artery thrombosis. Chest roentgenograms and a careful history are of great value.

Differentiation from coronary thrombosis is based on the history and the electrocardiographic, fluoroscopic and roentgenographic studies.

### *Case Report*

The following case was seen at the University Hospital and represents a fairly typical example of the syndrome.

A white male, age 52 years, was admitted to the University Hospital September 14, 1947, and died September 16, 1947. He gave a history of periodic episodes of cyanosis and dyspnea since childhood and the patient had been told that he had congenital heart disease. Except for occasional attacks of dyspnea and cyanosis, he was not incapacitated and was employed as a barber. There was no history of exertional dyspnea, but the patient had mild anginal pain for a long time and evening swelling of his feet. However, when the edema disappeared by morning, he attributed the swelling to his occupation.

In July 1947, the patient had a severe bout of dyspnea, cyanosis, and edema of his ankles. He was placed at bed rest and remained there for one week. Subsequently the edema disappeared and the cyanosis lessened so the patient started back to work for short periods of time.

On September 12, 1947, he noticed severe fatigue and when the dyspnea and cyanosis progressed in degree, the patient retired to bed. By September 14, 1947, he appeared at the hospital complaining of cough, marked dyspnea, deep cyanosis, mild ankle edema and a temperature of 101 degrees F.

On examination it was noted that the patient was in marked respiratory distress with deep cyanosis of the skin and mucous membranes. The lips and nail beds were particularly blue. There was no distention of the cervical vessels. The percussion note was flat over the lower left chest and the heart was enlarged to the anterior axillary line. The cardiac rhythm was regular, the rate was 100 beats per minute and the

blood pressure was 130 mm of mercury over 80 mm of mercury. A palpable systolic thrill was present in the second and third interspaces about 6 cm to the left of the mid-sternum and a very loud systolic murmur was heard in this area. The liver was palpable and there was mild pitting edema of the ankles.

On roentgenographic examination the film showed diffuse infiltration of the entire left lung with some infiltration in the right mid-lung field and in the right lower lobe. The urine was negative, the serologic test for syphilis was negative and complete blood studies were negative except for a 10 850 white blood cell count and a differential count showing 95 per cent polymorphonuclear leucocytes. The sputum cultures were positive for *Streptococcus viridans*, *Staphylococcus albus* and *Diplococcus pneumoniae* but repeated sputum cultures were only positive for *Escherichia coli*. The blood cultures were negative.

The electrocardiogram was not characteristic of any particular syndrome, but there were some aberrant T waves. The voltage was normal.

During the course of the disease the patient was treated with sedatives, penicillin and oxygen and although the temperature returned to 99 degrees F in 24 hours and the chest signs cleared, the dyspnea increased so that the patient was breathing at a rate of 35 excursions per minute. The cyanosis remained and gradually increased until the patient expired on September 16, 1947, two days after admission.

At necropsy the pathologist noted marked distention of the cervical vessels and deep cyanosis of the conjunctivae, nasal and oral mucosa and the skin of the upper and lower extremities. There was no pitting edema present but the liver was enlarged to 8 cm below the costal margin. The heart was enlarged with hypertrophy of the right ventricle and there was a patent foramen in the interventricular septum. In addition marked arteriosclerotic changes along with dilatation and tortuosity were present in the pulmonary artery. Bilateral thrombi were seen in the vessels at a point just proximal to the level of the first division of the right and left pulmonary arterial branches. The thrombi were large, markedly adherent and definitely laminated, causing the lumen of the vessels to be considerably reduced in size. Early organization was noted in and about the point of attachment of the thrombi to the arteriosclerotic vessels.

This case is an example of one of the more frequent possibilities by which pulmonary thrombosis develops. The patient gave a history and the physical findings of congenital heart disease which at autopsy was found to be a patent interventricular septum. As a result of the increased blood volume created by the patent septum, the right ventricle was hypertrophied and the pulmonary artery was dilated. Moreover the increased volume increased the pulmonary artery pressure, which ultimately resulted in arteriosclerosis and subsequent bilateral thrombosis of the pulmonary vascular system.

The arteriosclerotic process involved the main stem of the artery and its right and left pulmonary branches but it was not present below the level at which the right and left branches begin to divide into the various lobar vessels. The thrombi were attached

to the vessel walls over the arteriosclerotic plaques just proximal to the point at which the vessel divides into lobar branches. This is the usual site of formation and attachment, but in most cases the thrombus then builds in a retrograde fashion toward the heart. In this particular case the thrombus extended distally into the lobar branches, but they were not attached within these vessels. Because the main vessels were the points of origin, their lumina were materially blocked and thus the entire lung fields on both sides suffered a marked reduction in blood supply, producing the characteristic clinical syndrome.

This is an example of the type of case that Harvey and Hogg<sup>3</sup> had in mind when they stated that one must suspect the possibility of pulmonary artery thrombosis when a patient who has congenital heart disease suddenly develops a marked increase in the severity of his symptoms.

### SUMMARY

1) A resumé of the medical literature pertaining to the subject of thrombosis of the pulmonary artery and its right and left branches has been presented.

2) Pathologic changes associated with the condition have been discussed.

3) A definite clinical syndrome produced by such a thrombus has been described.

4) A typical case report, illustrating the syndrome, and substantiated by pathological material, was made.

### RESUMEN

1) Se ha presentado un resumen de la literatura médica tocante al tema de la trombosis de la arteria pulmonar y sus ramas derecha e izquierda.

2) Se han discutido las alteraciones patológicas asociadas a esta condición.

3) Se ha descrito el síndrome clínico bien definido que produce ese trombo.

4) Se presenta un informe sobre un caso típico que ilustra el síndrome y que fue verificado con tejidos patológicos.

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#### MOTION PICTURE SESSION AT ANNUAL MEETING

A new feature to be presented at the 15th Annual Meeting of the College will be a motion picture session to be held at the Ambassador Hotel, Atlantic City, on Friday evening, June 3 Interesting films dealing with problems of diseases of the chest will be shown Applications should include the title of the film author, approximate running time, whether silent or sound color or black and white, and the size of the film A brief resume of the material presented in the film should accompany the application

One evening has been set aside for the motion picture session and therefore only a limited number of films can be shown Applications for consideration in the program should be submitted at once to Dr Paul H Holinger, Chairman, Committee on Scientific Program, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois

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#### CORRECTION IN THE JANUARY ISSUE

David Salkin, M.D, F.C.C.P. of the Veterans Administration Hospital, San Fernando, California, completed work on his paper, "Postmortem Pneumothorax," at the Hopemount Sanatorium and the University of West Virginia Medical School, Morgantown, West Virginia

# College Chapter News

## FLORIDA CHAPTER

The Florida Chapter of the College will hold its first meeting at the Belleview Biltmore Hotel, Belleair, Florida, on April 10, in conjunction with the annual meeting of the Florida Medical Association, April 10-13. The meeting will open at 9 00 a m with an administrative session and election of officers. The following scientific program will be presented:

"Flight Medicine: Practical Experiences in Transportation of Ill Patients in Commercial Aviation,"

Howard K. Edwards, M D , F C C P

"The Role of X-Ray in Pulmonary Diseases" (Slide Demonstration),  
Maurice Kovnat, M D , F C C P

"Indications for Bronchoscopy, Chronic Asthmatic and Static Asthmatic,"

Nathaniel Levin, M D , F C C P

"Treatment of Lung Abscess,"

DeWitt C. Daughtry, M D

General Discussion

"X-Ray Symposium of Common Conditions Found in the Chest,"  
Physicians are requested to bring films on any problems in which they are interested. Unlimited discussion.

M. Jay Flipse, M D , F C C P , Moderator

The present officers of the Florida Chapter are Dr. E. C. Brunner, President, and Dr. Howard K. Edwards, Secretary-Treasurer. The Program Committee is comprised of Dr. Nathaniel Levin, Chairman, Dr. Arnold S. Anderson, and Dr. Alexander Libow.

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## ILLINOIS CHAPTER

The Illinois Chapter of the College held a dinner meeting and presented a scientific program at the Congress Hotel, Chicago on February 11th. The program presented was as follows:

"Photoelectric Plethysmograph and Direct Blood Pressure Measurement as an Aid in the Diagnosis of Coarctation of the Aorta,"

Melvin Goldman, M D , St. Louis, Missouri

"A Clinical and Pathological Correlation of Tumors of the Lung,"

Lauren V. Ackerman, M D , St. Louis, Missouri

"Arterial Venous Aneurysm of the Lung,"

Alfred Goldman, M D , F C C P , St. Louis, Missouri

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## POTOMAC CHAPTER

The Annual Meeting of the Potomac Chapter of the College will be held at the Sheraton Belvedere Hotel, Baltimore, Maryland, on April 27, in conjunction with the Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland, April 26-27. The chapter will present their scientific program on April 27 as a section of the Medical and Chirurgical Faculty of the State of Maryland. The program will be as follows:

*Title:* Neoplasms of the Chest

*Moderator:* W. LeRoy Dunn, M D , F C C P , Washington, D. C.

- Subjects* "Tumors of the Mediastinum,"  
 Edward M Kent, M.D , F C C.P , Pittsburgh, Pennsylvania  
 "Intra Pulmonary Neoplasms,"  
 Edgar W Davis, M.D , F C C.P , Washington, D C  
 "Tumors of the Thoracic Cage,"  
 John W Strieder, M.D , Boston, Massachusetts

Following this scientific program, the Potomac Chapter will have a business meeting and a cocktail party and banquet An X-ray Conference will be held immediately following the banquet Dr Otto C Brantigan, Baltimore, President of the Potomac Chapter, will preside at the banquet

### TEXAS CHAPTER

The Annual Meeting of the Texas Chapter of the College will be held at the Gunter Hotel, San Antonio on May 2nd The following program will be presented

- "Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis "  
 Robert G McCorkle, M.D , F C C.P , San Antonio  
*Discussant* Rodger J B Hibbard, M.D , Legion  
 "Experimental Massive Pulmonary Collapse,"  
 W W Coulter, Jr, M D , F C C.P , McAllen  
*Discussant* James E Dailey, M.D , F C C.P , Houston  
 "Important Aspects of the Relationship of Dust to Health "  
 M J Cuen, M.D , Galveston  
*Discussants* Charles M Hendricks, M.D F C C.P , El Paso,  
 John S Chapman, M.D F C C.P Dallas  
 John A Wiggins, M.D , F C C.P , Ft Worth  
 "The Early Detection of Primary Bronchogenic Carcinoma,"  
 Robert R Shaw, M.D , Dallas  
*Discussants* Howard T Barkley M.D Houston  
 Samuel H Haigler, M.D , Wharton  
 "Carcinoma of the Lung in Children and Young Adults '  
 John Roberts Phillips, M D , F C C.P , Houston  
*Discussant* Donald L Paulson, M D Dallas  
 "Anesthesia in Chest Surgery "  
 Raymond F Corpe, M.D , Sanatorium  
*Discussants* Robert R Shaw M.D Dallas  
 George W Waldron M.D , F C C.P , Houston

Dr Paul A Turner, Louisville, Kentucky, Chairman of the Board of Regents of the American College of Chest Physicians, will be guest speaker at the annual banquet His subject will be "Modern Trends in Treatment of Pulmonary Tuberculosis" Dr Turner will be introduced by Dr Elliott Mendenhall, Dallas President of the Texas Chapter of the College

The Wisconsin Chapter of the College held a meeting at the Medford Hotel Milwaukee on December 3rd Dr Douglas Guthell presented a study of "Twenty-Five Women Ill with Tuberculosis who had been Treated with Streptomycin "

### ANNUAL MEETING AMERICAN BRONCHESOPHAGOLOGICAL ASSN

The 30th Annual Meeting of the American Bronchoesophagological Association will be held at the Drake Hotel, Chicago Illinois April 18-19 1949



## MEDICAL SERVICE BUREAU

### POSITIONS AVAILABLE

Position open as assistant on sanatorium staff Will require good knowledge of collapse therapy and x-ray interpretation Person would also have to have duties in tuberculosis diagnostic clinic and in microfilm reading Please state all particulars concerning self together with qualifications Also state salary expected in addition to full maintenance Please address Box 191A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois

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Two residencies in tuberculosis available at sanatorium in California Accredited and approved All types of treatment for pulmonary tuberculosis including major chest surgery Salary depending on experience and personality Good quarters on grounds for both single and married persons Residents must secure California license and must be U S citizens Please address Box 193A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois

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Resident physician wanted for fully approved and accredited sanatorium in Indiana Full diagnostic, social and therapeutic services and active out-patient department Salary \$300 to \$400 monthly with complete maintenance Candidates must be eligible for an Indiana license Please address Box 194A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois

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Tuberculosis Staff Physicians Approved, modern hospital, 300 beds Metropolitan area All departments and modern facilities for diagnosis and treatment University affiliation Man or woman Good salary and complete family maintenance in new home American citizenship, graduate of approved American school, approved state licensure required Available before March 15, can employ at once An active service, excellent opportunity for an industrious physician Please address Box 195A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois

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Resident physician in tuberculosis sanatorium Training in all forms of collapse therapy Salary \$4,200 and complete maintenance for self and family Yearly salary increase and possibility to work up One year credit for boards in internal medicine granted Located in resort country University near for postgraduate training Please address Box 196A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois

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Resident physician wanted for 80-bed county sanatorium Active out-patient department One-year internship required Salary up to \$3,000 and maintenance Approved by A M A and College of Surgeons Macon County Tuberculosis Sanatorium, Decatur, Illinois

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Positions open for physicians in large tuberculosis hospital Salaries from \$4,800 to \$7,320 annually Contact Personnel Office, Battey State Hospital, Rome, Ga

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Position available for Assistant Medical Superintendent Tuberculosis Sanatorium To assist in administration of 100-bed tuberculosis sanatorium and out-patient chest clinic Some previous experience in a tuberculosis institution required Candidates must have a license or procure a license to practice in California before appointment Salary range \$549 to \$686 Apply Civil Service Commission, Court House, Redwood City, California

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### POSITIONS WANTED

Chest physician in Australia desires postgraduate training or permanent residence in sanatorium in the USA Experienced in the management of chest diseases especially tuberculosis, pneumothorax, pneumolysis, bronchoscopy and minor thoracic surgery Graduate of University of Sydney Please address Box 240A, American College of Chest Physicians, 500 N Dearborn St, Chicago 10, Ill

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Experienced chest physician, Fellow American College of Chest Physicians, desires position as assistant medical director of small sanatorium or hospital Please address Box 241A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois

# DISEASES *of the* CHEST

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## The Surgical Treatment of Mitral Stenosis (Mitral Commissurotomy)\*

CHARLES PHILAMORE BAILEY, M.D., F.C.C.P., F.A.C.S.\*\*

Philadelphia, Pennsylvania

Stenosis of the mitral valve has long challenged the therapeutic ingenuity of the medical profession. It has seemed unreasonable that young persons in otherwise satisfactory health should be condemned to a life of invalidism and early death. Success in treating strictures and stenoses in other organs has suggested that such a simple mechanical defect should not present an insuperable problem.

However, fear of surgical attack upon the heart, discouraging results of early attempts, and a general lack of appreciation among the medical profession of the extreme seriousness of this disease, have greatly hampered those interested in the problem. Many internists, among whom are cardiologists, feel that with proper medical management and limited activity these patients may live a normal span of life. It is true that most older practitioners know of a case or two of mitral stenosis which has survived to an advanced age. Unfortunately, these men do not have any roughly accurate idea of the much larger number of cases which have died at an early age. It is also notable that these same older patients will admit that they have not especially enjoyed their prolonged life of limited activity. The author has recently been consulted by a woman of 58 and another of 62 who have been "successfully" treated medically for 25 and 28 years, respectively. They now, at their advanced age, being no more limited than they were 10 years ago, are futilely petitioning for a chance at surgical relief.

The serious prognosis of mitral stenosis can hardly be properly

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\*Presented at the 14th Annual Meeting, American College of Chest Physicians, Chicago, Illinois, June 20, 1948.

\*\*Associate Professor, Thoracic Surgery, Hahnemann Medical College

presented statistically, since cases vary in severity, and since death is often wrongly attributed to some other heart condition, to asthma, or to pulmonary tuberculosis with hemorrhage. This latter syndrome (mitral stenosis with serious hemoptysis) has been shown by Wolfe and Levine in 1941<sup>1</sup> to have a mortality of 66 per cent within 3 years. This has been brought home dramatically to the author, who recommended surgery in two such cases eight and six weeks ago, respectively. Both at first accepted surgery and then changed their minds because of the presumed risk. Both have already died of pulmonary hemorrhage.

With such a dismal outlook, it is time to take steps to differentiate those cases which are mild or non-progressive from those who will not have any useful existence. It then is incumbent upon the profession to learn how to alleviate the severe cases.

Levine<sup>2</sup> has stated that the average period of time between the onset of the signs of congestive failure and death is four and three-fifths years. And this in the vast majority of cases appears in young individuals, between 15 and 30 years of age.

It is my belief that there are at least one million cases of mitral stenosis in the United States, one-quarter of which are suitable for surgery. This brings the problem of management within the domain of not only the cardiologists and internists, but also of every general practitioner.

The cause of disability and death in mitral stenosis is related to (1) right ventricular failure (congestive), (2) pulmonary vascular congestion leading to fibrosis, pulmonary edema, and hemoptysis varying from slight to fatal, (3) inability of the left ventricle to furnish sufficient blood to the body. The pulmonary vascular congestion is due to damming back of blood behind the stenotic valve, producing great distention of the left auricle and hypertension of the entire pulmonary vascular bed, especially on the venous side. These pulmonary symptoms are often most prominent and have led certain investigators to deviate from the direct line of approach to the pathology. Thus, the observations of Lutembacher<sup>3</sup> that cases of mitral stenosis associated with a congenital interauricular septal defect are clinically milder than those without such defects, have led to various attempts to produce such a defect. The production of such septal defects and of anastomoses between the azygos vein and a pulmonary vein (which accomplishes the same type of shunt) have been successfully accomplished experimentally both in our animal laboratory and others. It has remained for Dr. Richard Sweet<sup>4</sup> of Boston to actually perform such an anastomosis successfully in clinical human cases. The shunt permits the high pressure in the pulmonary veins and left auricle to be reduced toward an equilibrium with

the systemic venous pressure. Thus the pulmonary hypertension is markedly reduced with alleviation of all pulmonary congestive symptoms (hemoptysis, pulmonary edema). The patients with this pulmonary syndrome become more comfortable. Both Harken<sup>5</sup> and the author have opened the interauricular septum in human cases.

However, it must be remembered that the left auricular hypertension is really the main compensatory mechanism which helps force blood through the narrowed mitral orifice. The removal of this hypertension while it may relieve the most prominent symptoms, actually leads to a reduction in the amount of blood which passes through the valve into the left ventricle. Thus the reduced ventricular output is still further reduced and systemic congestion is somewhat increased by the shunt.

It appears that some procedure which would permit a greater amount of blood to enter the left ventricle must be the logical method of attack. This might be a plastic procedure upon the mitral valve (including dilatation, valvulotomy, or partial valvulectomy), or the insertion of a mechanical valve (plastic or metal) into the mitral ring, or some method of bypassing the valve entirely. This latter (bypassing) has been successfully accomplished in the laboratory by Litwak<sup>6</sup> who successfully communicated the left inferior pulmonary vein to the left ventricle by a free vein graft.

Of these methods, some type of plastic procedure upon the valve has seemed most promising. An open method of attack is at present hampered by the lack of a suitable mechanical pump to carry on the circulation during the operative procedure. However, Templeton, Gibbon, and Allbritten<sup>7</sup> have had some success by the open technic in animals. Furthermore, any involved or extensive plastic repair would probably break down by virtue of the necessarily constant cardiac function during the healing period. Thus a closed type of operation which permits continuance of normal circulation and accomplishes only a rather simple plastic procedure would seem to be most desirable at present.

A review of the reports in the literature by Cutler and Beck<sup>9</sup> in 1929 of operations upon the aortic and mitral valves revealed that of the first 10 cases of mitral stenosis subjected to operation, one died during insertion of an instrument into the left auricular appendage, two were subjected to finger dilatation of the mitral valve after insertion through the left auricular appendage (both cases lived and were improved), three cases were treated by tenotome division of a valve cusp (one lived 4½ years and was much improved), and five cases were subjected to partial valvulectomy by the cardiovalvulotome (all died).

It was interesting to note that of the two cases of manual dila-

tation of the valve reported, both survived the procedure and were improved. Of three cases of simple valvulotomy (cutting across a valve cusp), only one case survived. Of five cases of partial valvulectomy (by valvulotome), none survived. Since simple manual dilatation actually meant the partial tearing open of the fused portions of the valve commissures, it closely resembled the operative procedure which we are now presenting. Cutting across a valve cusp, on the other hand, would either produce little enlargement of the valve opening if of slight extent, or marked regurgitation if of great extent. Therefore, it would be either useless in alleviating the stenosis or extremely dangerous because of the production of sudden severe regurgitation. Partial valvulectomy as practiced with the cardiovalvulotome was a blind, crude procedure, frequently leading to severe unexpected damage to other parts of the heart, and even if successful in application, led to severe mitral regurgitation.

Allen and Graham<sup>9</sup> attempted to improve the control of valvulotomy by devising a cardioscope in 1923.

After 1929 no more surgical attempts were made until 1945. Both Dr. Dwight Harken<sup>5</sup> and Dr. Horace Smithy,<sup>10</sup> as well as the author, have made recent operative attempts to improve cases of mitral stenosis. Our clinical experience with the surgery of the mitral valve has been with five cases to date.

During the past eight years the author and his associates have performed diverse and repeated operations upon the mitral valve of some 60 mongrel dogs. Several conclusions have been reached: (1) The approach through the left auricular appendage is the most satisfactory one since there is less danger of arrhythmia, greater ease of entering the valve, and greater ease in controlling hemorrhage. Entrance through the apex of the left ventricle leads to more arrhythmia, greater difficulty in entering the mitral valve orifice because of impinging upon the chordae tendinae, and greater difficulty with hemorrhage. (2) Production of an appreciable degree of sudden mitral regurgitation is tolerated poorly by dogs. Thus extensive cutting of the anterior cusp of the mitral valve is nearly always attended by operative mortality. It would seem that regardless of the reported observation that clinical mitral regurgitation is less crippling than clinical mitral stenosis, these sick human hearts will not tolerate the sudden production of a large mitral regurgitation very well. (3) The accurate placement of an instrument to divide a mitral valve depends upon actually palpating the valve and instrument from within the auricle at the time of operation. Thus, whether the cutting instrument is inserted through the ventricle or auricle, it is necessary that the right index finger be passed through an incision

in the left auricular appendage to palpate the valve and cutting edge (4) The palpating finger is well tolerated in the left auricle and even within the actual valve orifice unless obstruction of the passageway is produced Thus, there is no particular danger in palpating the valve, and therefore blind surgery to the valve is no longer necessary (5) Dogs do not seem to develop mitral stenosis and the actual human type of pathology cannot be well reproduced in animals There is, therefore, a limit to the analogies between experimental and clinical studies (6) A considerable variety of instruments may be employed for commissurotomy We now prefer a backward cutting punch (Figure 1) and a scalpel with a hooked blade (Figure 2) With the experience gathered from animal work it remains only to reconsider the pathology of mitral stenosis to arrive at the most effective method of direct attack upon the stenotic valve

The pathology of clinical mitral stenosis varies In most cases it is due to rheumatic fever The valve cusps become thickened, shortened, and fibrotic The cusps appear to fuse at the commissures so that the opening becomes a shortened and narrowed slit in a thickened, fibrotic plaque Through this rigid slit a certain amount of regurgitation occurs At times there is calcification of the valve edges If the calcification is extensive it renders this plaque hard The calcification is often increased at one point, perhaps due to calcification of a former vegetation or verrucca Such a localized involvement may by itself obstruct two-thirds of the normal valve opening, and thus be responsible

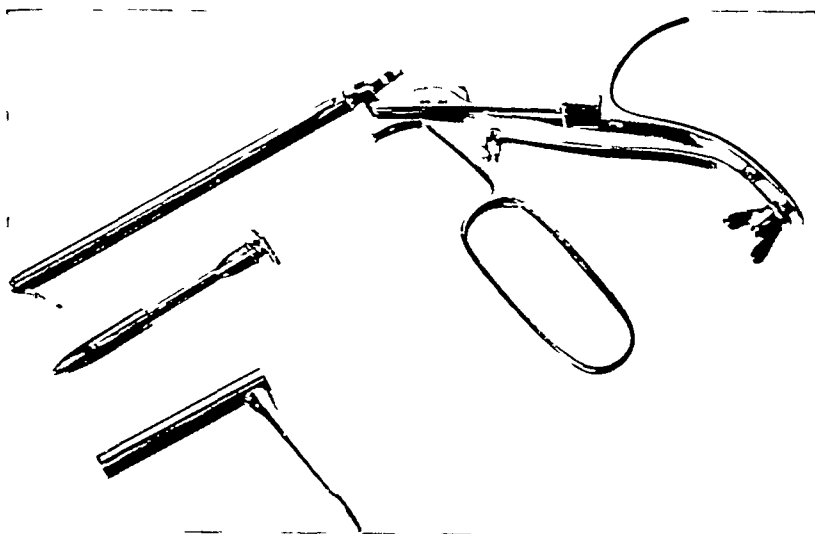


FIGURE 1 Backward cutting punch with trocar and cannula



FIGURE 2 a

FIGURE 2 b

FIGURE 2 c

Figure 2 a Right and left curved commissurotomy knives and cannula—Figure 2 b Commissurotomy knife in cutting position  
Figure 2 c Commissurotomy cannula on right index finger

for the stenosis of an otherwise not too distorted valve. An interesting and important observation at autopsy study of these valves is that the *plaque of thickened fibrotic tissue is surrounded by a margin of fairly normal valve tissue* (Figure 3). It occurred to the author that it might be possible to cut such a plaque completely in two by two incisions at the commissures of the valve.

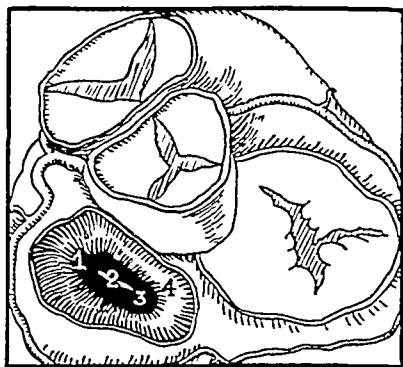


FIGURE 3 a

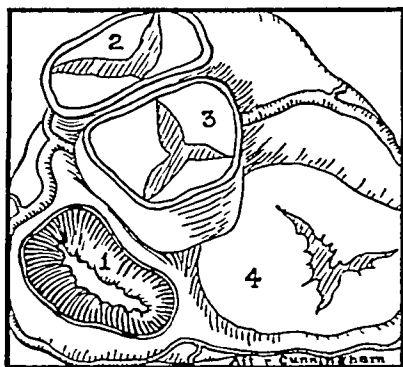


FIGURE 3 b

Figure 3 a Stenotic Valve 1) Lateral commissure 2) Mitral orifice 3) Fibrotic zone 4) Normal tissue—Figure 3b Normal Valve 1) Mitral valve 2) Pulmonary valve 3) Aortic valve 4) Tricuspid valve



FIGURE 4



FIGURE 5

Figure 4 Stenotic valve opened by lateral commissurotomy—Figure 5 Superior ventricular aspect of aortic cusp of mitral valve after commissurotomy showing maintenance valvular support by the chordae-tendinae



STATISTICAL TABLE OF OPERATIONS FOR CHRONIC VALVULAR DISEASE UP TO 1929

Case	Author or Operator	Date	Diagnosis	Method or Instrument	Results
1	Doyen	1913	Congenital pulmonary stenosis, patent inter-ventricular septum	Tenotome	Died few hours after operation
2	Tuffier	1914	Aortic stenosis	Finger dilatation	Recovery, improved
3	Cutler and Levine Boston M & S J 188 1023, 1923	5/20/23	Mitral stenosis	Tenotome	Died, 4 years and 6 months after operation
4	Allen and Graham	8/ 7/23	Mitral stenosis	Cardioscope	Operative death
5	Cutler, Levine & Beck	10/ 7/23	Mitral stenosis	Tenotome	Died, 10 hours after operation
6	Cutler, Levine & Beck	1/12/24	Mitral stenosis	Tenotome	Died, 20 hours after operation
7	Cutler, Levine & Beck	2/25/24	Mitral stenosis	Cardiovalvulotome	Died, 6 days after operation
8	Cutler, Levine & Beck	6/11/24	Mitral stenosis	Cardiovalvulotome	Died, 3 days after operation
9	Souttar	5/ 6/25	Mitral stenosis and aortic insufficiency	Finger dilatation	Recovery, living and improved
10	Pribram	11/14/25	Mitral stenosis and aortic vegetative endocarditis	Cardiovalvulotome	Died, 6 days after operation
11	Cutler & Beck (first report)	12/ 8/26	Mitral stenosis	Cardiovalvulotome	Died, 15 hours after operation
12	Cutler & Beck (first report)	4/15/28	Mitral stenosis	Cardiovalvulotome	Died, 3 hours after operation
		TOTALS	12 cases 1 aortic stenosis, acquired 1 pulmonary stenosis, congenital 10 mitral stenosis, acquired	2 finger dilations 4 tenotome attempts 5 cardiovalvulotome attempts 1 cardioscope attempt Mortality, 83 per cent	

opening (Figure 4) These incisions should be extended well into the normal valve tissue margin so that the two halves of the plaque could separate freely, being hinged by soft valvular tissue at either extremity In the pathologic specimens such incisions appeared to accomplish this result It was also apparent, since the chordae tendinae were left intact (Figure 5), that increase in fluid pressure on the ventricular side would force the rigid halves of the valve together, while increase in fluid pressure on the auricular side would cause them to separate It seemed that such incisions could relieve a mitral stenosis without increasing the amount of regurgitation which already existed because of the rigid valve opening

### CASE REPORTS

*Case 1* Our first clinical case was W S, a man of 37 years who had been severely incapacitated for 16 years and who had had several severe episodes of hemoptysis On November 14, 1945 his left anterior chest was opened through the third left anterior interspace at Hahnemann Hospital, Philadelphia, Pennsylvania The pericardium was opened and the distended left auricular appendage practically herniated out of the pericardial sac A purse-string suture was placed around the tip of the auricular appendage preparatory to inserting a trocar and cannula for passage of the backward cutting punch As the trocar and cannula were inserted the purse-string suture was pulled upon and tore out of the friable and distended auricular appendage Severe bleeding occurred and a large clamp was hastily applied to the appendage close to its origin The clamp was completely closed—and cut through the appendage wall Attempts to reapply a clamp proximally were temporarily successful, but it was impossible to get mattress sutures to hold in the friable auricular tissue under tension enough to approximate the edges of the auricular defect The patient died on the operating table of hemorrhage, no valvulotomy having been performed We have ever since realized that the human auricular appendage in mitral stenosis is friable and entirely unlike that of a normal dog We no longer permit a hemostat to be closed on an auricular appendage beyond the first tooth of the ratchet, and prefer not to actually close the ratchet

*Case 2* Our next case was W S, a 29 year old married female who had been a cardiac invalid for 11 years, and who had been in congestive failure on several previous occasions during the preceding 7 years On this occasion she failed to respond to the usual medical measures and remained in a precarious state with engorged liver and ascites in spite of digitalis and mercurial diuretics Since she was deemed hopeless, her physicians felt that she might be subjected to valvulotomy At operation on June 12, 1946 the heart was approached through a left anterior thoracic incision, and the pericardium was incised Up to this point the blood pressure was approximately 60/50 mm mercury, and the surgeon began to seek an honorable way of abandoning the procedure However, the medical consultants stressed that she would undoubtedly die from the anaesthesia and exploration unless some relief of the stenosis could be obtained Therefore, the left auricular appendage was entered by

trocar and canulla, and the backward cutting punch was inserted through the canulla. It was well tolerated by the heart, but could not be inserted through the mitral valve orifice. Several firm irregularities were encountered by the instrument but no mitral opening could be found. Therefore, the trocar and canulla were removed, the opening in the auricular appendage was enlarged, and the right index finger was inserted. The mitral valve was found to be a tiny slit which would not admit the tip of the index finger. There was considerable calcification about the valve mouth. This had been palpated by the instrument, but the actual orifice was too small to admit the punch (about the size of a small lead pencil). The valve was forcibly dilated digitally, so that the finger could be inserted into the orifice to the second phalangeal joint. Care was taken not to obstruct the opening for longer than three heart beats at a time. The valve appeared to tear open at both commissures. The thrill which was prominent prior to dilating the valve, immediately disappeared. The blood pressure promptly rose to 80 systolic and the patient's condition began to improve. Because of the improvement and the desperate nature of the risk, the finger was withdrawn and the auricular appendage ligated without any attempt at incising the valve.

The patient's condition continued to improve so that the blood pressure was 130 systolic at the conclusion of the procedure. The diastolic murmur of mitral stenosis was entirely gone subsequent to surgery, but a systolic murmur appeared. Some felt that this might be due to mitral regurgitation, but the author is doubtful. Improvement was continued for 30 hours. After that the condition began to deteriorate and she died rather quickly 48 hours after surgery. Autopsy revealed a greatly dilated heart, 300 cc of serous fluid in the pericardium, and some plastic pericarditis (sterile). The mitral valve showed evidence of having been torn open at both commissures, but the tears had not extended into the normal marginal valve tissue. The torn surfaces had therefore not separated much, and had become agglutinated by fibrin which accumulated in the orifice and gradually reduced the effective mitral opening to probably a smaller size than that existing at the time of operation. It was difficult to imagine any degree of regurgitation through that valve orifice. No anticoagulant therapy had been employed. As a result of the autopsy findings, the idea was conceived of performing what had been later termed "commissurotomy" by Dr. Thomas Durant of Philadelphia.

*Case 3* The next patient was W W, a white male 38 years of age, who had been having episodes of severe hemoptysis over a period of 1½ years. In fact, he had had a segmental resection of the right lung performed for bronchiectasis one year previously, in the belief that his hemorrhages were of pulmonary origin. However, after 8 months his hemorrhages had returned in an exsanguinating form. Re-study then revealed that a marked enlargement of the heart had taken place during the interim and typical evidences of severe mitral stenosis were now evident. The patient was also showing early signs of decompensation. On March 22, 1948 at the Memorial Hospital in Wilmington, Delaware, the left 4th anterior rib was removed and the pericardium was opened. Pressure in the left auricular appendage was 240 mm H<sub>2</sub>O. The auricular appendage was incised and the right index finger was inserted. The mitral valve was found to be obstructed mainly by a hard calcific nodule roughly 15 mm square which occupied the medial 2/3 to 3/4 of the mitral orifice. A marked presystolic thrill was present. The rest of the valve orifice was

non-calcified and leathery. It was too tight to permit insertion of the finger tip. A non-detachable knife with a curved handle was inserted along the dorsum of the palpating finger within a second glove until it perforated the end of this outer glove (Fig 3). It was then guided by the finger to cut the lateral commissure of the mitral valve orifice. The shape of the knife blade permitted it to repeatedly disengage from the valve, but it was possible to markedly loosen the valve opening. The author was somewhat dissatisfied by the amount of opening, but the calcified nodule prevented any incision on the medial commissure. Since the finger could now readily enter the ventricle, and since the thrill had completely disappeared, the finger was withdrawn and the auricular appendage was carefully oversewn. The patient's condition remained excellent throughout the operation. There was no arrhythmias, and the only weakening of the radial pulse was during actual obstruction of the valve by the finger. Continuous electrocardiograms during the operation showed only minimal abnormalities. Procaine (1/10 of 1 per cent) was administered by drip during the operation.

Because of the bitter experience with the previous patient, it was decided to use anticoagulant therapy. Therefore, the clotting time was kept at between 20 and 30 minutes by a continuous drip of heparin in saline. The patient did reasonably well until the second postoperative day, when evidence of hemorrhage into the left pleura required repeated thoracenteses. Heparin therapy was discontinued. When the red blood count had dropped to 2,450,000 on the third postoperative day it was felt necessary to transfuse him, and this was done, 2600 cc blood being given. Unfortunately, there was a misunderstanding regarding orders pertaining to fluid balance, and a total of 7,400 cc of fluid by mouth and parenterally on the fourth postoperative day, and 1,500 cc on the fifth postoperative day was administered. As a result the patient became markedly edematous. At about 4 p m he suddenly developed pulmonary edema and expired. Autopsy revealed over 1,000 cc of blood in the left pleura, a dilated heart and extensive pulmonary edema. The hemorrhage had apparently occurred from the chest wall in spite of extreme care in hemostasis during the chest wall closure. The auricular appendage had not bled and was completely occluded by a well attached thrombus (a constant finding in dogs subjected to this operation). The incision in the lateral margin of the mitral valve was approximately  $\frac{1}{4}$  inch in length and did not extend completely through the fibrotic plaque. There was no fibrinous sealing off of the valve orifice.

In reviewing this case, we considered that the following errors had been made: (1) Perhaps the use of the heparin therapy was unwise, since it had required the administration of a considerable volume of fluid, and since it undoubtedly played a major role in the secondary intrapleural bleeding. (2) The use of saline rather than glucose solution as a vehicle for the heparin. (3) Inadequate incision in the lateral commissure of the valve, partly due to the repeated disengaging of the knife blade on account of its shape. The medial commissure could not be cut because of the large calcification. (4) Unwise and excessive fluid therapy. (5) Perhaps accepting a case for surgery who had had diminished contralateral lung function from previous disease and partial lung resection. It was the consensus, however, of all physicians concerned that if we had just returned the patient to bed postoperatively, and not treated him, recovery would have followed.

*Case 4* The next case was J R , a 32 year old white male who had had advanced mitral stenosis for 7 years During the past 1½ years he had been in chronic congestive failure, although ambulant much of the time Digitalis and mercurial diuretics did not completely control the congestion Since his prognosis was extremely grave without surgery, it was finally decided to attempt a commissurotomy On June 10, 1948 at the Philadelphia General Hospital he was anesthetized with endotracheal ether and oxygen He was placed in the face-down position and the left posterolateral incision was made It was difficult for the anesthetist to maintain adequate oxygenation because of extremely limited vital capacity The 5th rib was removed and the thorax entered through its bed The lung was totally and extensively adherent to the chest wall, diaphragm, and pericardium These adhesions were carefully dissected free and the lung was retracted upward The pericardium was incised anterior to the phrenic nerve Procaine (1/10 of 1 per cent) was administered by intravenous drip (20-80 drops per minute) 2 per cent procaine was flushed in the pericardium However, the least touching of the heart, either ventricle or auricle, was followed by frequent extrasystoles and other irregularities Because of this extreme irritability of the myocardium, no attempt at valvulotomy was made The surgeon became worried and suggested abandoning the procedure at that time The staff felt that this would be the last opportunity for surgery to be utilized in this man Intravenous atropine did not relieve the myocardial irritability, nor did 50 mgm doses of procaine intravenously Intravenous quinidine was administered slowly by personnel experienced in its use Before completion of the injection the heart rate had become slow, so the quinidine was discontinued The systoles became weaker and stopped

Immediate manual massage restored regular contractions which ceased after a few minutes Massage was repeated After that, various stimulants, venesection, artificial respiration, etc , were used After the heart had been revived by massage a number of times and had failed as many, it was suggested that he might improve if the left ventricular output was increased by opening the mitral valve Since all was already lost, the auricular appendage was opened and the left index finger was inserted into a tight mitral orifice containing calcium deposits It was widely dilated, and the finger withdrawn No instruments were used The auricular appendage was ligated After massage had again reestablished a temporary heart beat, it was evident that the left ventricle had become considerably enlarged However, in spite of repeated massage and all recognized forms of drug stimulation, no permanent restoration of cardiac function could be accomplished At no time did ventricular fibrillation supervene

Autopsy was obtained and revealed considerable fibrosis of the myocardium but no evidence of Aschoff bodies nor active rheumatic myocarditis Since activity of the rheumatic process was not responsible for the extreme myocardial irritability we must look elsewhere for an explanation In view of the pleural adhesions and the thickened fibrotic lung tissue, and in consideration of the anesthesia difficulties, it is the author's opinion that hypoxia of the body generally and the heart specifically was probably responsible

We do not consider this a death attributable to mitral valve surgery, since death and an irreversible state had apparently become established well before a last ditch emergency dilatation of the valve was performed

Undoubtedly this man was too bad a risk for mitral surgery. The pre-operative ballistocardiogram had revealed a poor cardiac output, increased only slightly on exercise.

*Case 5* C W, a 24 year old white housewife, had been known to have a heart murmur for 17 years and mitral stenosis for 24 months. She had had gradual and progressive onset of dyspnea on exertion and had an attack of congestive failure in November 1947. Since that time she had been on extremely limited activity and received a daily maintenance dose of digitalis. On May 17, 1948 she was admitted to Episcopal Hospital in Philadelphia for study preliminary to a possible mitral commissurotomy. She had a typical loud presystolic mitral murmur and thrill. Interestingly enough, all of her clinical and laboratory studies, including ballistocardiography *at rest*, revealed fairly normal conditions. However, she did show marked enlargement of the left auricle (Fig 5), and was limited in exercise tolerance. The full extent of this limitation was not appreciated until the ballistocardiographic studies were repeated after exercise. Dr. Gordon Ring of the Physiology Department of Temple University was then able to show that her maximum cardiac output on exercise was only double that of her resting needs. Normally cardiac output on exercise will increase many fold. It is our belief that ballistocardiographic studies at rest and on exercise are the only truly dependable objective means of evaluating the functional status of the heart in mitral stenosis. Venous pressure was 111 mm H<sub>2</sub>O. Circulation time 12 minutes arm to lung and 20 minutes arm to tongue. Operation was performed on June 10, 1948. The left anterolateral approach was chosen and the 3rd rib was resected. The pericardium was opened anterior to the phrenic nerve. Pressure in the left auricle was 280 mm H<sub>2</sub>O. Procaine 2 per cent was applied in the pericardium. Procaine (1/10 of 1 per cent) was given by continuous intravenous drip. The auricular appendage was opened and the right index finger covered by two gloves, was introduced. Between the gloves was a special hooked knife with malleable handle (devised since our experience with case 3). The mitral valve was found to be small, just admitting the tip of the finger. It was not calcified and had a leathery feel, more like kid-skin than cow-hide. It was displaced high up anteriorly. The hooked knife was inserted through the valve orifice and engaged on the lateral commissure under direct digital guidance. The knife was then drawn backward an inch, widely dividing the commissure. The finger was now inserted through the cut valve and some fine remaining fibrous strands were broken up. The valve was now widely patent. The finger was withdrawn and the auricular appendage ligated. The chest wall was closed with drainage. The entire operation had taken 80 minutes. During the period of cutting and dilating the valve, the blood pressure fell and the heart function became slow and labored. No arrhythmia developed. Enlargement of the left ventricle was immediately evident. No anticoagulant or postoperative intravenous therapy was permitted.

Postoperatively the previously marked presystolic murmur was absent. A pericardial friction rub was present on the first and second days postoperative but was gone by the third. She was out of bed on the third day, and walking the fourth. Her greatest difficulty was inability to void for four days postoperatively. On the seventh postoperative day the patient had no cardiac murmur audible to the author. The pulmonic second

sound remained accentuated. She was asymptomatic and felt she was better than she had been for years.

Because of her evident good condition she was transported without incident by train to a 1,000 mile distant medical convention for presentation in person.

No murmur is now present.  $P_2$  is still loud. She is ambulant and comfortable. Unfortunately, it is too early (8 days postoperative) to repeat the ballistocardiography on severe exercise.

(February 1, 1949. Patient is continuing to do well 7½ months subsequent to surgery. She is now able to perform all her own housework. Her ballistocardiographic studies reveal marked improvement in cardiac output on exercise. The  $P_2$  is much less prominent. She has taken no digitalis for 5 months.)

### SUMMARY AND CONCLUSIONS

1) Surgical technique and methods and anesthesia have now advanced to the point where intracardiac manipulations may be undertaken with reasonable safety.

2) The mitral valve is best approached through the left auricular appendage by an anterolateral approach. Approach through the apex of the left ventricle is less desirable, in our opinion.

3) Accurate surgical maneuvers depend upon control by vision or digital palpation. In closed surgery of the mitral valve digital palpation through an opening in the left auricular appendage is the logical method of control.

4) Commissurotomy enlarges a stenotic mitral valve orifice and permits valvular function without an appreciable increase in the pre-existing amount of mitral regurgitation.

5) Three cases of mitral valve surgery are presented with one survivor who shows a gratifying early postoperative result. One other case could undoubtedly have been salvaged with our present knowledge, and one case probably was too advanced to help. Two cases of mitral stenosis in which surgery was planned and started but not completed are described.

6) We believe that the operation of commissurotomy has great value in certain cases of mitral stenosis. The selection of cases should undoubtedly be limited to those with essentially single valve lesions in which all rheumatic activity is healed. It is doubtful in the present state of our knowledge whether cases in chronic or acute congestive failure should be operated. Certainly results will be poorer in this group. One of the most urgent indications for surgery is hemoptysis, especially if severe.

7) We believe that commissurotomy is preferable to a shunt operation (azygos-pulmonary vein anastomosis, or opening of the interauricular septum), because the latter merely relieves pulmonary symptoms by destroying one of the natural compensating mechanisms. What is the gain if the signs and symptoms of pul-

monary congestion are relieved and yet the patient goes on to systemic circulatory failure? Or if the left ventricular output is so reduced by loss of its compensating mechanism that the patient's physical activities are still more limited? However, in a hypothetical case where the opening of the valve might not sufficiently reduce pulmonary congestion (due perhaps to too limited incision of the valve commissures) we would not hesitate to perform such a shunt if the pulmonary symptoms endangered life. It is our belief that a high pressure in the left auricle is helpful postoperatively in maintaining separation of the valve cusps after commissurotomy. If a shunt is performed before the valvular surgery, there is undoubtedly a much greater tendency for the raw edges of the commissure to seal together and re-establish the mitral stenosis.

8) We feel that preoperative digitalization, quinidinization, and the use of intravenous procaine during surgery are valuable in supporting cardiac function and in preventing arrhythmia. Antibiotics are given to prevent infection of the wound and of the cut valve surfaces (subacute bacterial infection). Apparently anticoagulant therapy is dangerous and unnecessary.

9) We believe that ballistocardiography before and after exercise offers us the best single objective measure of ventricular output and reserve.

February 1, 1949. Since this time, 5 additional patients have been subjected to this operation. Two are doing very well. One died 2½ months after surgery. One died of an error in technique at operation (cutting across a valve leaflet). One did very well for 6 days but died suddenly of a cerebral arterial embolus. Clotting had occurred in the sutured left auricular appendage. We now ligate the appendage at the base to prevent this.

### RESUMEN Y CONCLUSIONES

1) Las técnicas y los métodos quirúrgicos y la anestesia han avanzado hasta tal punto que es posible llevar a cabo manipulaciones intracardiacas con razonable seguridad.

2) La mejor vía de entrada a la válvula mitral es a través del apéndice auricular izquierdo en una dirección anterolateral. En nuestra opinión es menos deseable entrar a través del vértice del ventrículo izquierdo.

3) Las maniobras quirúrgicas exactas dependen del directo control visual o del palpamiento digital. En la cirugía cerrada de la válvula mitral, el método lógico de control es el palpamiento digital a través de una abertura en el apéndice auricular izquierdo.

4) La comisurotomía ensancha el orificio de la estrecha válvula.



mitral y permite que funcione la válvula sin aumentar apreciablemente el grado de insuficiencia mitral pre-existente

5) Se presentan tres casos de cirugía de la válvula mitral con un sobreviviente que ha mostrado un resultado postoperatorio temprano satisfactorio. Con nuestros conocimientos presentes es indudable que se habría podido salvar a otro caso, pero el tercero probablemente estaba demasiado avanzado para que se le hubiera podido ayudar. Se describen dos casos de estrechez mitral en los que se intentó y se comenzó la cirugía pero no se la completó.

6) Opinamos que la operación de comisurotomía es muy valiosa en ciertos casos de estrechez mitral. Es indudable que se debe limitar la selección de los casos a aquellos que presentan lesiones esencialmente univalvulares en los que ha cesado toda la actividad reumática. En el estado actual de nuestros conocimientos se duda que se deba intervenir en casos de insuficiencia cardíaca congestiva aguda o crónica. Naturalmente que los resultados serían peores en ese grupo. Una de las indicaciones más urgentes para la intervención es la hemoptisis, especialmente si es grave.

7) Opinamos que la comisurotomía es preferible a una operación de desviación (anastomosis de las venas azygos y pulmonar, o abertura del séptum interauricular), porque esta última operación solamente alivia los síntomas pulmonares mediante la destrucción de uno de los mecanismos compensatorios naturales. ¿Qué se gana con aliviar los signos y síntomas de la congestión pulmonar cuando el paciente va a parar en la insuficiencia circulatoria general? ¿O si se reduce hasta tal punto la cantidad de sangre que expela el ventrículo izquierdo, por la pérdida de su mecanismo compensatorio, que se limitan aun más las actividades físicas del paciente? Empero, en un caso hipotético en el que la abertura de la válvula no redujera suficientemente la congestión pulmonar (debido quizás a la incisión muy limitada de la comisura de la válvula) no vacilaríamos en ejecutar una operación de desviación si los síntomas pulmonares amenazaran la vida del paciente. Opinamos que la hiperpresión en la aurícula izquierda en el periodo postoperatorio ayuda a mantener la separación de las cúspides de las válvulas después de la comisurotomía. Si se ejecuta una operación de desviación antes de la cirugía valvular, no hay duda de que existe mayor tendencia a que los bordes vivos de la comisura se unan de nuevo y reestablezcan la estenosis mitral.

8) Nos parece que la digitalización y la quinidización preoperatorias y el empleo de procaina por la vía intravenosa durante la intervención son valiosas en ayudar la función cardíaca y en evitar las arritmias. Se administran antibióticos para evitar la infección de la herida y de las superficies cortadas de las válvulas.

(infeccion bacteriana subaguda) Aparentemente la terapia anti-coagulante es peligrosa e innecesaria

9) Creemos que la balistocardiografia, antes y después del ejercicio, nos ofrece la mejor medida objetiva para medir la reserva y la cantidad de sangre que expela el ventriculo

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## D I S C U S S I O N

EVARTS GRAHAM, M.D., F.C.C.P.

St Louis, Missouri

It is thrilling to be here this afternoon and see this patient demonstrated by Dr Bailey I congratulate him very much indeed on his success He was kind enough to refer to me as being one of the pioneers in this work It was 25 years ago, in 1923, that Dr Duff Allen and I published our first report on surgical attempts to cut the mitral valve This was done by means of an instrument to which he referred, which, however, I am afraid he perhaps slandered a little by saying that it did not give more than a fleeting glimpse of the valve As a matter of fact this instrument gives one very satisfactory vision, of any valve or any part of the heart with which it is in contact It is based on the principle of a convex lens which pushes the blood away, just as one can see his finger in a glass of milk, for instance, if he pushes the finger against the side of the glass—it pushes the milk away and one can see the finger with all the lines on it and all details That is the principle of the cardioscope which we devised We operated successfully on a large number of dogs, making holes of various sizes in the mitral valves, depending upon what we were anxious to make I agree fully that too large a mitral regurgitation is fatal even in the dog with a normal heart

However, we created less degrees of mitral regurgitation in dogs many times—perhaps 50 dogs—and had them live for a long time still retaining their mitral regurgitation but able to undertake any sort of activity. We had some of these dogs live for a period of two years and then sacrificed them in order to see the condition of the heart.

Then we tried the procedure on a patient. Unfortunately, as with any new surgical procedure, the pioneers get only the patients who are the worst possible risks. Perhaps that is as it should be, there should be a certain amount of conservatism, but it seems sometimes as if our medical conferees are much too conservative about permitting the surgeon to apply a procedure which seems perfectly logical. This patient on whom we operated in 1924 was a bad risk, and she died shortly after her mitral valve had been cut. The approach was made through the auricular appendage.

I am much pleased to have this work revived by Dr. Bailey and Dr. Smithy and others, and feel certain that mitral stenosis and, in fact, stenosis of other valves, is a condition which can be corrected by surgical intervention. I don't think there is much doubt about it but I believe we are going to have to get suitable patients, we are going to have to inform our medical colleagues that it is a feasible operation and that patients must be referred, if any are going to be referred, who are not practically moribund already. On the other hand, we should not feel, necessarily, that present methods available are going to be the ideal ones, there are certainly going to be many modifications of the procedure of approach to these valves. Although I was as much thrilled as anyone here at seeing this beautiful result, I feel that we must postpone final judgment about such results until after a period of time—perhaps a year—has elapsed, because we found 25 years ago, and I think others have found since, that sometimes these valves which are cut have a tendency to heal over again and revert to their former condition. I was also much interested in the demonstration by Dr. Smithy of the great value of the intramural injection of cocaine. That is new to me, applying it within the muscle of the heart, and I think it is likely to be a procedure which will be of inestimable value in all cardiac surgery.

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GORDON MURRAY, M.D.  
Toronto, Canada

I wish to thank you very much for extending me the courtesy of the floor. I have enjoyed very much the papers on this subject, and my comments relate to experimental work which I did a good many years ago and reported at that time. This work was based

on the "inference" in the discussion this afternoon, namely, that division of a mitral valve may produce regurgitation, if it is a satisfactory division, and secondly, it might heal if it is divided only. Working on that assumption I thought the best idea would be to take out the diseased valve and replace it with a good one. We did that experimentally in a large group of animals in which the controls died but those with the artificial valve survived, when we had completed the operation satisfactorily.

I had hoped to postpone what I am about to say for about a year, but it would appear I am faced with saying it now. I have operated on two patients in whom I have taken out the lateral cusp of a stenosed mitral valve. Both patients were in a bad way because of mitral stenosis. A new valve was placed in each case, and they are both alive. The first one, done a few years ago, was an Indian. He disappeared later on and I don't know what happened to him. For a time, however, I know he was well, but now I can not find him as he is in the North country. The second case was operated on very recently. The patient is quite well. I do not know yet that he is benefited, nor how he is going to be, but in any case he survived and perhaps he is improved.

The method, is to take out one cusp of the valve with a punch, much as was described this afternoon. We also made a cardioscope very similar to that described by Dr. Graham, and I can assure you we can see fairly well what we want to see. It is a small field, but by shifting it around more can be seen. After having taken out the valve—we have the new valve handy—the patient very quickly begins to show some effects of regurgitation. The new valve is, I suppose, the same as you would use. A section of the cephalic vein is turned inside out so that its intima is lying in the blood stream. The palmaris longus tendon is put down the lumen of the valve to give it some substance and strength. It is then passed from before aft through the heart on the ventricular side of the site of the original valve, so that on systole it is jammed back into the opening left by resection of the valve, on diastole it floats out of the opening so that it is not an obstruction to filling of the ventricle. It seems to work satisfactorily.

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HORACE G. SMITHY, M.D.

Charleston, South Carolina

The ramifications of this subject are of such magnitude as to prohibit consideration of the various phases in the time allotted for discussion. Therefore, I have selected one technical aspect in particular, namely, the control of cardiac arrhythmias occurring

during operation upon the valves of the heart This can best be presented by a motion picture which will be shown subsequently

We have performed eight operations for mitral stenosis in seven patients with two deaths It is significant that the fatalities occurred in the second and third cases, the last five being done consecutively without serious complications as our technique gradually became better standardized The early results in our series, while by no means brilliant, have been sufficiently encouraging to warrant pursuing this study further We feel that the procedure can be accomplished in the future with increasingly good results and with a significant decrease in mortality

*(Motion Picture)* These are excerpts selected from a complete motion picture record of the technique of experimental aortic valvulotomy in dogs developed during the past two years in the experimental laboratories of the Medical College of South Carolina You will note in the first procedure, in which no attempt has been made to protect the animal against arrhythmias, that both ventricular tachycardia and ventricular extrasystoles were prominent features of rhythmical disturbances which occurred during placement of the purse-string suture in the cardiac apex and during passage of the valvulotome into the chamber of the left ventricle Quite obviously, arrhythmias of this sort occurring in a human patient whose myocardium has been damaged by rheumatic fever might be the cause of an immediate fatality As noted in the second procedure, 5 per cent procaine is being applied topically over the surface of the heart and is allowed to pool in the pericardial sac so as to bathe the epicardium generally Observe now, the series of ectopic beats which occur following stimulation of the apex by a blunt instrument, indicating little or no protection by the topical procaine This study has been repeated in a large series of animals, we have been unable to confirm the findings of others pertaining to the protective action of topical procaine against rhythmical disturbance

In the third procedure, you will note that 2 per cent procaine solution is being infiltrated into the myocardium of the apex at the point where the purse-string suture will be placed and the valvulotome passed I should like to emphasize that the procaine injection which you see on the screen is actually an intramural infiltration and not an intracardiac injection Now watch closely and I am sure that you will agree that no ectopic beats and no evidence of tachycardia or fibrillation are to be seen during the successive series of stimulation of the infiltrated area by the blunt instrument This procedure also has been investigated thoroughly in the laboratories and has uniformly protected successfully each animal against the occurrence of arrhythmias

In each of our human cases in whom a ventricular approach has been selected, intramural procaine infiltration has been used as a routine I am pleased to report that we have not encountered a serious disturbance of rhythm in any of our patients to date

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### *Closing Remarks*

*Charles P Bailey, M.D., F C C P* You see what happens when you discuss something you don't know about' I did not know you could see very well with the cardioscope, but from the pictures in the original article I did not think it would afford good vision

Naturally, we must wait for a year before evaluating the procedure I believe that since the intra-auricular pressure is elevated, that when the commissures are cut, the valve will stay opened In dogs which are permitted to survive one year after surgery there is no tendency to healing of incisions of the valve

No one said anything about the lack of heart murmurs and pre-cordial thrill in this girl To my ears there are none, and most people agree with me, but there have been about 10 per cent who thought they could hear a presystolic murmur and some also a systolic murmur I am sure it is not enough for most of you to recognize, and hope it will not increase It is certainly remarkably different from the loud presystolic crescendo type murmur with prominent thrill which existed preoperatively

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# The Importance of Continued Studies in Tuberculosis\*

HERBERT L. MANTZ, M.D., F.C.C.P.  
Kansas City, Missouri

Two men had just completed a golf game and were adding their scores. A second twosome approached, walked across the green and one of them asked "How did you fellows score?" 1st Twosome "83 and 85. What were your scores?" 2nd Twosome "85 and 88." 1st Twosome "Pretty close to us. We were watching you but we didn't think you were playing as we never saw you hit a ball." 2nd Twosome "Oh we don't use balls. We know where they would go."

This very fantastic golf story is quite apropos when we think of some medical practices. The problem of using controls in therapy is not new and this is no time to go into all of its phases. I feel that it is important enough for us to give it some thought now, because we have for the first time drugs which are effective and also because surgical procedures are changing rapidly.

Progress in the treatment and control of tuberculosis moved at a comparatively leisurely pace during the past when we contrast it with the greatly accelerated tempo of these days. The inter-relationship of all scientific fields has had its effect upon the therapy of tuberculosis. In the last decade, the greatly stimulated effort in the field of antibiotics has presented new opinions and new problems to the field of tuberculosis research. New ways must be found to tackle an old problem, that is, to determine quickly and accurately the value of any pertinent discovery in the treatment of tuberculosis.

Let us look for a moment at the ways in which these answers traditionally have been found. A new form of therapy is tested by a man here and by another there, a few cases treated here and a few there, good results here, poor results there. This is essentially a trial and error approach and it does seem that there should be something better, something more orderly, which would give us a correct answer sooner. Perhaps the answer is essentially the same whether we arrive at it in one year or in 20 years. Tuberculosis therapy is measured in years, not months or days, and during these waiting years many things happen to people with

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\*Address of the President of the Southern Chapter, American College of Chest Physicians. Presented at Miami, Florida, October 24, 1948.

this disease. If we can hasten the process of acquiring knowledge, we as physicians, should let nothing deter us.

Therapy in tuberculosis has always been guided by what is called "clinical judgment." This intangible factor is affected by many variables, and the most important of these is past experience. Dr. Hertzler once said that "calves suckled by the same cow were quite likely to act alike." Thus, clinicians trained with certain chest surgeons will have fewer qualms about recommending pulmonary resection than those with a more conservative background. We know about these differences of opinion and, in fact, welcome them, for they keep alive the open-mindedness and healthy discussion necessary to any science. But, we must remember that our various shades of "clinical judgment," differing as they do, are not a proper yardstick to measure the worth of any form of treatment.

In tuberculosis therapy there are many procedures which are conceded to have value. First is the basic one, bed rest. Next, are artificial pneumothorax and pneumoperitoneum, usually considered as medical procedures. Last are the surgical measures, phrenic crush, thoracoplasty and pulmonary resection. All of these are useful, but there is considerable difference in opinion as to when to use them, singly or in combination. Such divergence of thought is often disclosed in any sanatorium conference where two or more persons are free to express opinions. Such differences are good proof that we lack the carefully analyzed reliable experience necessary to develop sound judgment. It is true that we need experience to develop good judgment, but unfortunate that too often experience is gained by bad judgment.

Five years ago the tri-state area of Michigan, Wisconsin and Minnesota began a yearly conference at Pembine, Wisconsin. The most popular method of presentation has been to have a representative hospital from each state show a series of consecutive cases, at least 50 in number. Cases are chosen from one to two years back so that follow-up is possible. These three states have always been rather close in their medical relationships. If any geographical area is united in a therapy program this one should be. The surprise of the first conference was the great difference of professional opinion exhibited. To date no group has presented any study with a controlled series, and probably the chief value of such meetings has been the intensive review of cases by the individual hospitals where the cases were prepared for presentation, plus the benefits gained by observing results from other places. These conferences have been extended to other sections and have been valuable in improving clinical judgment but they have not yet provided the factual material so badly needed.



However, a start has been made to secure more facts, and because it is a significant start I should like to make a few comments about the Streptomycin Evaluation Program of the Tuberculosis Study Section of the National Institute of Health. This cooperative program began actually too late psychologically, in the case of streptomycin, because many clinicians had already formed definite clinical impressions of what the drug could accomplish and were, therefore, unwilling to let chance decide whether any particular case would or would not receive streptomycin. However, in evaluating another therapeutic agent we need not be too late as we can use this procedure before such clinical impressions, false and true, are established.

The question of the usefulness of streptomycin in the treatment of tuberculosis was first attacked by members of the Chemotherapy Committee of the American Trudeau Society, to whom the producers of the new antibiotic supplied a large amount of the drug for clinical investigation. Some of the ablest and more experienced tuberculosis clinicians in the country carried out these investigations which resulted in a number of suggestive findings. These studies provided no definitive answer as to the exact place of streptomycin in tuberculosis therapy, since there was no control group against which to measure the status of the streptomycin treated patients. It is clear, however, that the experience gained in these studies was valuable in setting up the large-scale program of the Tuberculosis Study Section for the evaluation of streptomycin. There are now three studies in progress pertaining to pulmonary, military and meningeal, and skeletal tuberculosis. The pulmonary study is the largest and since principles on which it is based illustrate the use of the control principles, it is sufficient to describe this alone. A detailed protocol outlining uniform procedures for all investigators was issued. Definite diagnostic criteria were established and each participating hospital submitted cases which it considered suitable for study. Cases submitted could be treated by bed rest, any type of surgery, or collapse measures. In submitting cases, the investigators said in effect "These are cases in which I am willing to let administration of streptomycin be determined by the play of chance. I will provide any other treatment indicated to both those receiving and those not receiving streptomycin." The cases submitted are reviewed by a Selection Panel which determines the suitability of cases on the basis of the criteria established by the protocol, i.e., proved bacteriology and capable of significant improvement without streptomycin and excluding cases of minimal tuberculosis. The suitable cases are then divided by a purely random method into a treated and a control group and the hospital is bound by this decision.

If the value of a drug is completely unknown, there can be no logical objection to the establishment of a control group. Unfortunately, when this study was set up favorable "clinical impressions" of streptomycin treatment were already flourishing. Some provision had to be made, therefore, for the control patient who did so badly that it could be argued that no other therapy would be of any help, and that streptomycin might. With the controls who developed miliary or meningeal tuberculosis, the problem was simple. Past experience overwhelmingly showed that they would die without the new drug, and treatment could be started on these cases without delay. It was more difficult, however, to define the type of patient who, although not doomed with certainty, was so obviously losing out in his battle with the infection that he could reasonably be considered a "gone goose." Such patients were presented to a central "Appeals Board." The approval of this board was necessary before the patient could be treated with streptomycin.

Tuberculosis is a relatively slow moving disease. To really know what any given form of therapy is doing, it is necessary to watch a group of cases for a long time, not weeks, or months, but years. Since this is a long time job and it was obvious that paper work could develop to be an impossible chore, it became necessary to ask what we were really trying to find out, and in what order. It seemed to us that in the case of streptomycin we were trying to determine what the end result was, how two groups of patients, one receiving the drug and one not, compared at the end of the year. By placing the entire emphasis on the end result, it has been possible to request only periodic reports. If there are notable differences between the treated and the control group, then the other step must be taken, the determination of the mechanics or the significance of the changes taking place in tuberculous patients. Great stress has been laid upon uniformity and those items which are not at present susceptible of accurate measurement have not been collected, even though it is recognized that such factors as psychosomatic level undoubtedly are important in the progress of any particular patient.

Most of you have probably read the British report of a cooperative study of miliary and meningeal tuberculosis, published in the *Lancet*, April 17, 1948. An impressive body of evidence has been accumulated from a relatively small number of cases. I say "relatively" because here in America we have had much freer access to the drug, and have treated many more cases, yet when they are grouped together they justify only the most general conclusions. Why? The answer is that the British conducted a carefully regulated study in which comparable data were collected

from each case. For instance, a question arose as to the necessity of intrathecal treatment. The problem was attacked simply by withholding intrathecal streptomycin from a random group who were in other respects similar to the rest of the patients in the study. When it became apparent that these patients were faring much worse than their intrathecally treated fellows, the question was answered. This is an example of the effective use of the control principle.

With the appearance on the scene of an increasing number of new antimicrobial agents, each a "wonder drug" at first glance, we must learn to use this principle in a steadfast manner, or bog down in confusion.

The evaluation of this material is going to teach us a good deal, not only about streptomycin, but about tuberculosis, and about ways of doing cooperative studies in the future. I cannot emphasize too strongly the great stumbling block that terminology is in our present state of tuberculosis research. We must find ways of describing our clinical material so clearly that others will know exactly the kind of cases we are talking about. We must also find ways of describing the changes which take place in a year in the x-ray films of a chest so that we can know what happened without streptomycin, what happened only with streptomycin and what we failed to achieve with either.

Only meager results are available at this time, but it is interesting to note that, while the streptomycin groups appear to be markedly superior to the non-streptomycin group at the end of three months and have still an edge at six months, at nine months after beginning of treatment there appears to be practically no difference between the two groups. Reports on more cases must be accumulated before definite conclusions can be drawn.

This method of developing factual data can and should be used to evaluate some of the older but still controversial methods of therapy. When a new procedure is begun it should be tested against one which experience has valued.

Pneumoperitoneum with or without phrenic crush, and phrenic crush to supplement bed rest are two procedures always likely to provoke discussion. If we are to know which is the better we should treat series of patients concurrently, with the only variant being the procedure in question.

The use of lucite balls for extra-pleural plumbage is exciting much interest. Experience gathered from a few places ranges from uncontrolled enthusiasm to the other extreme of definite rejection of the method. With this procedure there are usually two choices. Collapse by surgery is considered advisable. We have to decide between thoracoplasty and an extrapleural operation.

Once we have decided that operation is to be done and that either one of the two procedures may be done, decide by chance and so develop two series of cases. In no other way can we come to a definite opinion. It is not scientifically sound to compare present surgical results with those of the past as surgical technique, anesthesia, preoperative and postoperative care are constantly improving. In the Veterans Administration, surgeons at first considered it necessary to use streptomycin to cover all thoracoplasty cases. Using alternate case methods they found this was unnecessary and it is doubtful if it is advisable to use it routinely in pulmonary resection. But until parallel case studies are made we will not be sure. I see no reason for not testing experimental or new procedures against tried and known ones. We can only argue about pneumoperitoneum until we have compared the procedure with bed rest by the alternate case method. When this is done perhaps skeptics may be convinced, or enthusiasts quelled.

The American College of Chest Physicians is interested in Tuberculosis Research. I believe that most of us realize the necessity of obtaining more basic knowledge of tuberculosis and we are interested in placing therapy on a better foundation. The alternate case method described should be as applicable to surgical problems as it has been in studying streptomycin. The Tuberculosis Study Section of the National Institute of Health has shown us that a cooperative study involving several different hospitals is practicable. I hope in the future that some of you will be interested in this problem, use this method of approach and find the answers to some of our questions.

In conclusion, I am reminded of a story which is all too true of many a sanatorium conference. A boat at sea ran into a severe storm. At last the captain decided to anchor, "Throw out the anchor!" he ordered. "We can't, Captain, there is no rope on the anchor." "Throw it out anyway, it may do some good."

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# Early Diagnosis as the Means of Tuberculosis Control

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Although tuberculosis has been known for many centuries, it is only in the past few decades that great strides have been made toward its conquest. This has come about largely through the development of methods by which recognition of the disease in its earliest stages can be achieved. The results are two-fold: (1) Isolation of contagious patients from individuals not contaminated. (2) Treatment of patients at a time when the greatest rate of recovery can be expected. The cases in this report may help to illustrate the effectiveness of control by the early diagnosis and supervision of students presenting evidence of having been infected with tubercle bacilli.

At the University of Minnesota, with an enrollment of approximately 27,000, the vast majority of students are in the age range of 17 to 30 years. It is in this period that tuberculosis kills more individuals annually than any other disease. The program of control at the University of Minnesota has two main objectives.

The first is the detection of the disease in any student who might be infected. The status of each entering student in relation to tuberculosis is determined. At the time of the physical examination required on admission to the University, a routine photofluorogram of the chest is made on all students. Within a period varying from one or two days, to two or three months after the initial examination, a tuberculin test, Old Tuberculin 1-1000, is applied and read in 72 hours. If the student reacts to the tuberculin, a second photofluorogram of the chest is done, and if this film indicates the possible presence of pathologic changes, a 14 x 17 inch chest x-ray film is made. If this reveals any abnormality, the student is immediately referred to the chest clinic in the Health Service, for further study.

As a result of this procedure, many of the cases of tuberculosis found among University students are of the primary infection type. The tuberculin test has proved an invaluable aid in determining the status of an individual in relation to tuberculosis. The routine photofluorogram is also of great help. There is, however, a change in the reaction to the skin test before there are significant roentgenographic findings.

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The second objective in the control of tuberculosis is the supervision and rehabilitation of tuberculous patients as found among the student body. In this report are presented nine cases that represent the variety of situations that are seen in attempting to control this disease among students. With a large school of nursing, both undergraduate and public health nursing, as well as a large medical school, our total incidence of tuberculosis is higher than universities that do not have these two colleges.

*Case 1* A 21 year old girl entered the school of nursing on January 2, 1945. The general physical examination revealed slight obesity, and the Mantoux test 1-1000, was negative. In the summer of 1946 she had been exposed to a contagious tuberculous patient in the hospital. She was tested in the fall of 1946 and found to be a reactor. Six 14 x 17 chest x-ray films from the time of entrance to the University to the 19th of March 1947 were reported negative. When seen in April 1947, a 14 x 17 chest x-ray film was requested in three months. In July 1947, a 14 x 17 roentgenogram revealed a small shadow in the right lung at the level of the 4th interspace anteriorly, which was suggestive of a tuberculous lesion. Subsequently, she was x-rayed in September 1947, November 1947, and in January 1948 the changes previously mentioned remaining stationary. Three gastric lavage specimens were obtained in September 1947, but no acid fast bacilli were detected by guinea pig inoculations. The sedimentation rate was not significantly elevated. The girl has carried on her activities in the school of nursing under careful observation. There has been no progress of the disease.

This case probably represents first infection type of tuberculosis, although no tubercle bacilli were reported on gastric analysis or sputum examination. It is difficult to say without qualification that this lesion represents a primary infection in view of the fact that a period of more than one year lapsed from the time of a negative to a positive test. A primary infection may have developed, the lesion noted on the x-ray films appearing as a reinfection type of tuberculosis. It has been pointed out that it is "impossible" to locate the initial lesion in the majority of young adults who become infected with the tubercle bacillus. There is little room for doubt, however, that a definite reaction to tuberculin is an indication of the presence of tubercle formation somewhere in the body. This particular case serves to illustrate the value of doing skin tests on students of nursing and medicine at least every six months. It is only in this way that a lesion can, with certainty, be suspected as a possible tuberculous infection.

*Case 2* A 22 year old male entered the University on September 19, 1946 and received an entrance physical examination. He did not react to 0.1 milligram of tuberculin and a photofluorogram of the chest was reported as negative. In May 1947, he was still a non-reactor and routine periodic health examination was also reported as negative. A second photofluorogram of the chest at that time was negative. In October

1947, he came to the dispensary because of pain in the left anterior chest which was made worse by deep breathing. Physical examination revealed no abnormalities. Four days later he complained of marked weakness and persistence of the pain in the left chest. Physical examination revealed dullness and absence of breath sounds in the left lower lung field, and he was admitted to the hospital. The clinical impression of pleurisy with effusion was confirmed by x-ray film and he reacted strongly to 0.1 milligram of tuberculin. Pleural fluid and gastric lavage specimens did not reveal tubercle bacilli either on culture or guinea pig inoculation. In spite of this negative laboratory data, the diagnosis of tuberculosis was considered probable in view of his change in reaction to tuberculin. Inasmuch as this man was not producing any sputum, it was felt that he could safely be sent to his home for a protracted period of bed rest under the care of his physician. He has continued to improve on bed rest at home and plans to return to the University.

This case illustrates again the importance of a change from negative to positive reaction of the skin test. Although one would strongly consider tuberculosis as the most probable cause of pleurisy with effusion in a young man, it is well known that other conditions can produce this clinical picture. If the tuberculin test in this case had been made positive by previous inoculation with BCG vaccine, the likelihood of a tuberculous pleurisy might not have been given due consideration and a loss of valuable treatment time could have resulted.

*Case 3* An 18 year old girl entered the school of nursing in September 1944. From October 1944, to February 1947, she was tested with tuberculin, both 0.1 and 1.0 milligram every six months and did not react. During February and March 1947, she was sent to a tuberculosis sanatorium for a part of her course of study. A 14 x 17 x-ray film of the chest in March 1947, was interpreted as negative. In the early part of June 1947, 0.1 milligram of tuberculin produced a strong reaction. An x-ray inspection of the chest at that time revealed an infiltrative lesion in the right cardiophrenic sinus with linear infiltration from this area towards the hilus of the right lung. The roentgenologist's report stated that the lesion strongly suggested either a lymphoblastoma or a mediastinal Hodgkin's disease. The evidence in favor of tuberculosis, however, was heightened by the change of the tuberculin reaction from negative to strongly positive within a 6 month period. The final diagnosis was tuberculosis, probably of the primary infection type. The patient was hospitalized and acid fast bacilli were demonstrated in gastric lavage specimens on two occasions.

Here again, the change of reaction from a negative to strongly positive is of inestimable value in the establishment of an early diagnosis. The primary impression of the x-ray department had been lymphoblastoma or possibly Hodgkin's disease with tuberculosis as a third possibility. If the tuberculin test is discarded as a diagnostic procedure, there is a risk of infectious cases remaining undiagnosed until their sputum becomes positive for tubercle

bacillus and the disease has advanced to the point where a much longer period of treatment is indicated

*Case 4* An 18 year old male entered the University in September 1946. There was no personal or family history of tuberculosis. A photofluorogram of the chest then and another in May 1947 were reported as negative. In this case, there is no record of whether he had had a previous tuberculin test at the time of his entrance to the University, and for some unknown reason he was not tested after admission. In December 1947 he had an x-ray picture done at the time of the chest survey in St. Paul, Minn. An infiltrative lesion in the left subclavicular area was found. Subsequent films in January 1948, again showed the lesion and it was concluded the infiltration was due to atypical pneumonia, infected lung cyst or abscess, with the possibility of a reinfection type of tuberculosis. Stereoscopic films a short time later revealed evidence of cavity in the subclavicular region on the left. It is likely that the lesion was present six months previously which was a short time after the photofluorogram of the chest had been reported as negative. The basis for this statement is the fact that a cavity with a wall as thick as the one seen rarely develops in less than six months. Tubercle bacilli were demonstrated in the sputum. The diagnosis of advanced pulmonary tuberculosis was made. The student withdrew from school and arrangements were made for hospitalization.

If a tuberculin test had been done when the patient entered the University, a more careful observation of the student would have taken place, and the lesion, perhaps, would have been discovered at an earlier stage.

*Case 5* An 18 year old girl entered the school of nursing in January 1945, at which time she did not react to 1.0 milligram of tuberculin. Subsequent tests applied every six months were negative until May 1947, when she reacted to 0.1 milligram of tuberculin. Since that time this girl has had chest x-ray films approximately every three months which have revealed no evidence of tuberculosis.

This patient, then, represents the most common response of the young adult who was a non-reactor and subsequently becomes exposed to and infected with tubercle bacilli. In this respect the response is identical to that seen in infants and children who are similarly exposed.

*Case 6* An 18 year old girl entered the school of nursing in October 1942. The family history and past history of the patient revealed no tuberculosis. The physical examination showed no significant physical defects and she did not react to 0.1 milligrams of tuberculin. Subsequently from March 1944 until May 1945, she was given tuberculin tests, 1.0 milligram of tuberculin every six months but did not react. After completion of her training on a large tuberculosis service, a tuberculin test was applied in the latter part of January 1946, and found to be strongly positive. X-ray films of the chest in February 1946, were reported as negative. However, in that month she reported to the dispensary because of pain in the left side of the chest which had been



present for two weeks This pain was made worse by deep breathing Examination on this first visit revealed no pulmonary pathologic changes However, the pain persisted for a period of about 3 weeks, and in March 1946, she was found to have a temperature of 100 degrees F She was admitted to the hospital and a series of x-ray films were taken On March 25, 1946, a chest roentgenogram showed a mediastinal mass, areas of increased density in the left lung field above the diaphragm and in the middle portion and the left hilar shadow was noted to be greatly enlarged Five days later, a chest x-ray film showed the same findings, with the conclusion that sarcoidosis was the most likely diagnosis

On April 6, 1946, another chest x-ray film showed findings which caused question of a primary type of tuberculosis of fairly extensive nature to be raised The patient was not producing any sputum, but three gastric lavage specimens produced tuberculosis in guinea pigs After two weeks of hospitalization at the Students' Health Service, the patient was discharged to her home on a regime of strict bed rest under the care of her private physician It would not seem too illogical to surmise in this case that had it not been for the change in the tuberculin reaction from negative to positive, the diagnosis of tuberculosis might not have been made until it became apparent that there was considerable spread of the process

*Case 7* This girl entered the University in September 1945, at the age of 20 and gave a history of having been a reactor to tuberculin since 1941, at which time one Indian boy and two other students in her high school class developed active tuberculosis Two of these cases were known to be contagious In the fall of 1941 she developed pleurisy with effusion Inoculation of pleural fluid into a guinea pig resulted in tuberculosis in the animal She was in bed at home for about one year and remained out of school for two years

X-ray studies of the chest at the time of admission to the University revealed a rectangular shaped homogeneous shadow lying laterally in the lower lung field which was thought to be a markedly thickened pleura Comparison with films taken elsewhere in 1942 and 1943 revealed the same shadow which confirmed this impression She has had chest x-ray films at regular intervals throughout her stay at the University, the most recent one being in February 1948, and there has been no change in the appearance of the chest

This case is an excellent example of the development of tuberculosis Earlier, in the very year in which she contracted the disease, she had been declared the 4H Health champion at the Minnesota State Fair when she was a non-reactor to tuberculin The sequence of events is important There is a history of known exposure with subsequent reaction to tuberculin Within one month after the test had been made, she developed the tuberculous effusion

*Case 8* A 28 year old graduate nurse entered the school of public health nursing in September 1947 She reported a previous tuberculin reaction When a photofluorogram of the chest was taken at the time of her entrance examination, a repeat examination was requested by the x-ray department because the first one was unsatisfactory The second

photofluorogram of the chest was done on December 2, 1947, and revealed some linear densities in the right lung. Subsequent history revealed that she had a mild cold in September of 1947, accompanied by slight pain in the right side of her chest on deep inspiration. This subsided in a few days. She continued to feel well until December 2, 1947, when she had a recurrence of the pleural pain. Because the pain in the thorax persisted, she returned to the dispensary on December 5th. Again physical examination revealed no chest pathology. On December 9th, physical examination revealed definite evidence of pleural effusion and she was admitted to the hospital. A 14 x 17 chest x-ray film confirmed the presence of pleural effusion with adhesions and pocketing on the right, but no parenchymal lesions could be clearly defined. A tuberculin test was applied and found to be strongly positive in 48 hours. Pleural fluid was aspirated and inoculated into guinea pigs but resulted in development of no tuberculous lesions. She remained in the hospital for a period of 26 days during which time the amount of fluid in the right base gradually decreased until at the time of discharge the lung fields on both sides appeared clear by x-ray. During hospitalization she ran a daily temperature elevation and the sedimentation rate was consistently and significantly elevated. She was transferred to another hospital for further treatment.

This case points out the importance of periodic observations for the development of a tuberculous effusion in a known reactor. This, of course, becomes doubly important in the case of a nurse or a medical student.

*Case 9* A 22 year old man entered the University in September 1946, at which time he stated that he was a reactor to tuberculin. A photofluorogram of the chest at that time was negative. On September 28, 1947, he was admitted to the Students' Health Service Hospital because of pulmonary hemorrhage of two days duration. Further history revealed that he had had a "cigarette cough" for about a year and a half. This, he had noted, was worse in the morning and productive of a moderate quantity of thick, foul-smelling sputum. Approximately six months prior to admission to the hospital, he had reported to the Minneapolis Public Health Center because of hemoptysis. No evidence of tuberculosis was found at that time after careful roentgenography, laboratory studies and physical examination. On May 22, 1947, a photofluorogram of the chest at the Students' Health Service once again was negative.

In view of the history, a tentative diagnosis of bronchiectasis was made and an x-ray film done on September 28, 1947, showed infiltration of the right base which was interpreted as a pneumonitis superimposed on a pre-existing bronchiectasis. Repeated sputum examinations were done and were reported as negative until October 3, 1947, at which time large numbers of tubercle bacilli were found in a specimen of sputum. On October 9, 1947 another chest x-ray film was made which revealed a probable bronchogenic dissemination of tuberculosis throughout both lungs. It was felt that streptomycin therapy was indicated and arrangements were made for admission to the Veterans Hospital, where he is making a very good recovery.

This case serves to illustrate again the importance of keeping the possibility of tuberculosis infection ever present in our minds.

## COMMENT

The advantages to the patient and to the community, of making the diagnosis of tuberculosis at the earliest possible time, are self-evident. The only way, at present, to eliminate this disease is by the diagnosis and treatment of the very early tuberculous patient before he becomes contagious. If he becomes contagious, he should be isolated as long as he is capable of transmitting the disease to others. This is as true of communities and states as it is of the University, for certainly universities represent small communities. With the advent of the routine photofluorogram, a valuable method was added to our fight against this disease. However, as the above cases illustrate, the tuberculin test is an important part of any tuberculosis control program. The importance of the routine testing of all University students cannot be overemphasized. It is equally desirable in the general practice of medicine, to test patients routinely, unless they have previously been found to react to tuberculin.

In his very excellent report of the situation among college students in Texas, Johnson has set forth the general objectives of a college control program as being three in number: 1) to determine the status of each student upon admission, 2) an annual tuberculosis survey of the resident student body, and 3) medical supervisory control of all rehabilitated tuberculous patients. At the University of Minnesota the first and third of these objectives have been put into practice. The second is at present applied to students of nursing and medicine.

## SUMMARY

The result of conducting a fundamental tuberculosis control program is a reduction in the incidence of this disease. In the past six months, in this "fair-sized community" of students, there have been found only about 20 new cases. The majority of these are at a very early stage and, for the most part, are now under treatment. Certainly, until there is a method developed that will insure true immunity to this disease, the use of the Mantoux test should be continued as it is the one diagnostic procedure which will tell those individuals who have been infected with tuberculosis and therefore need careful supervision.

## RESUMEN

El resultado de llevar a cabo un programa fundamental para el control de la tuberculosis es la reducción en la frecuencia de esta enfermedad. En esta colectividad bastante grande de estudiantes sólo se han descubierto 20 nuevos casos en los últimos

seis meses La mayoría de ellos se encuentran en un período muy temprano y la mayor parte están ya bajo tratamiento Seguramente que hasta que se desarrolle un método que asegure una verdadera inmunidad contra esta enfermedad, se debe continuar el uso de la prueba de Mantoux, pues este es el único procedimiento diagnóstico que indica cuáles son los individuos que han sido infectados con tuberculosis y que, por consiguiente, necesitan cuidadosa vigilancia

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# Diagnosis of Cancer of the Lung by the Cytologic Method\*

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The application of the fixation and staining technique developed by one of us (Papanicolaou)<sup>1 2</sup> in the study of sputum for cancer cells was first used by us June 22, 1945 The material was procured from a patient whose symptoms were those of a man who was discharged from the United States Navy in April 1945 as a psychoneurotic His routine chest plate was reported as negative He had a chronic, so-called "tobacco" cough, anorexia, insomnia, restlessness, nervousness and weight loss On June 5th, 1945 he coughed up a small quantity of blood and a chest x-ray examination revealed an infiltrative lesion in the right upper lobe with nodes along the right mediastinal border Bronchoscopy and bronchial washings were negative Sputum smears showed typical cancer cells Subsequent exploratory operation revealed an inoperable bronchogenic carcinoma (Figures 1, 2 and 3)

Since the above date, over 1,300 cases have been studied The specimens were procured primarily from patients of the New York Hospital and the Memorial Hospital A monograph is now under preparation in which a description of the cytologic findings and a statistical analysis of the diagnostic accuracy of this method will be given In a tabulation of 298 cases already reported in the American Journal of Public Health,<sup>3</sup> the accuracy was approximately 95 per cent for the positive reports (Classes IV and V)† and 85 per cent for the negative (Classes I and II) Of the cases reported as suspicious (Class III), approximately 50 per cent proved subsequently to be positive

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†Smear reports have been given on the basis of the following classification

*Negative,*

Class I Absence of atypical or abnormal cells

Class II Atypical cells present but without abnormal features

*Suspicious,*

Class III Cells with abnormal features suggestive but not conclusive for malignancy

Class IV Cells and cell clusters fairly conclusive for malignancy

Class V Cells and cell clusters conclusive for malignancy

The technique of preparing and staining smears from sputum may be summarized as follows

Sputum is expectorated directly for examination or put immediately into 70 per cent alcohol, in order to secure a good fixation and preservation of the cells. It is then spread on slides which have been previously coated with a thin film of Mayer's albumen. The smears are immersed, while moist, in equal parts of 95 per cent alcohol and ether, for at least thirty minutes. They are then stained in hematoxylin, OG6 and EA65, following procedure No 267<sup>14</sup>

Aspirated bronchial secretions and bronchial washings are mixed immediately with an equal volume of 95 per cent alcohol and ether



Figure 1a and 1b Case L1 Photographs of x-ray plates showing enlarged nodes in right hilar region

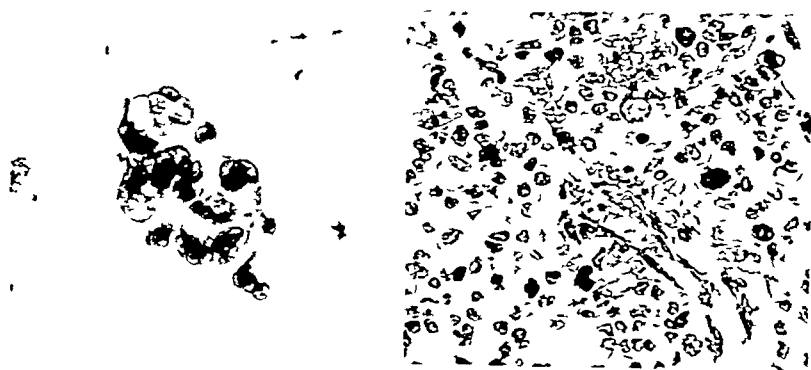


FIGURE 2

FIGURE 3

Figure 2 Case L1 Sputum smear Cluster of malignant cells Photomicrograph X285—Figure 3 Case L1 Section of node from hilus of right lung showing bronchiogenic carcinoma Photomicrograph X285 (Courtesy of the Pathological Laboratory of St Luke's Hospital)

and centrifuged for thirty minutes at medium speed. Smears are made from the sediment, fixed promptly in equal parts of 95 per cent alcohol and ether and stained by the same method as the sputum smears.

During the early phase of the work, most of our examinations were limited to a single sputum specimen. Repeat sputum specimens and aspirated bronchial secretions or washings were made available to us in a relatively small number of cases. We now request repeat specimens as well as aspirated bronchial secretions or washings in all cases in which smear findings have been negative or suspicious. In some instances, more particularly in the early cases, the number of exfoliated cancer cells may be small and the chance of missing a positive case greater if only one specimen of either type is examined.

The clinical value of the cytologic method is demonstrated by the fact that in many instances of pulmonary neoplasm, it furnished the primary diagnosis or the only preoperative histologic positive evidence. Over twelve pneumonectomies have been performed at the Memorial Hospital and the New York Hospital with a Class V smear report as the only positive preoperative histologic evidence to justify surgery.

The diagnostic value of the cytologic method is exemplified by the following two cases.

*Case 1* D W, L959, Male, 50 years old

*Symptoms* (1) Virus pneumonia, August 1947 (2) Recurrence, December 1947 (3) Slight cough (4) Pure culture, Monilia, January 1948

*Physical Examination* (1) Moist rales, right posterior lateral base (2) Old right apical tuberculosis



Figure 4 a and 4 b, Case L959. Photographs of x-ray plates showing infiltrative process in base of right lung.

*X-ray Report* Infiltration in right lower lung fields Findings seem most consistent with an inflammatory process (Figure 4)

*Bronchoscopy* Entirely negative

*Bronchial Washing Smear* (Figure 5) reported as follows "Conclusive evidence of a malignant neoplasm Malignant cells are numerous Class V"

Pneumonectomy was performed After the operation the smear became negative

*Gross Specimen* Basal portion of lower lobe is almost completely replaced by large, moderately firm tumor mass

*Section of lung* (Figure 6) Carcinoma of lung Grade II Peripheral bronchiolar type, having papillary and pseudoglandular features

*Case 2* W M, L593, Male, 56 years old

*Symptoms* (1) Chest pain for 8 months (2) Chronic cough (3) Sputum, profuse (4) Weight loss of 14 pounds

*Physical Examination* Suppressed breath and voice sounds in right lower chest

*X-ray* (Figure 7) "An endobronchial tumor as well as bronchiectasis must be considered"

*Bronchoscopy* Entirely negative

*Bronchial Washings* (Figure 8) "Conclusive evidence of a malignant neoplasm, most likely a bronchogenic carcinoma Class IV-V"

Pneumonectomy was performed

*Gross Specimen* Infiltrating tumor mass is seen at the bifurcation of the right lower lobe bronchus

*Section* (Figure 9) Bronchogenic epidermoid carcinoma Grade III The extrapulmonary nodes show no tumor

Diagnosis by the cytologic method is based on the identification of malignant cells which may appear either singly or in clusters Small fragments of tissue in the form of cell clusters are found frequently in cancer smears The criteria are, therefore, cytologic as well as histologic Of the cytologic criteria, the most pathog-

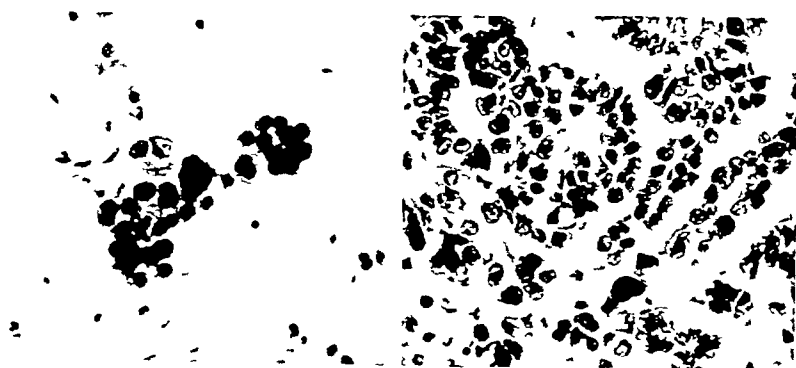


FIGURE 5

FIGURE 6

Figure 5 Case L593 Sputum smear Cluster of malignant cells Photomicrograph X285—Figure 6 Case L593 Section of tumor of right lung showing carcinoma of lung grade II Photomicrograph X285 (Courtesy of the Pathological Laboratory of Memorial Hospital)



nomonic are those related to changes in the size, form and consistency of the nucleus. In certain types of carcinomas, as the epidermoid, cancer cells display striking structural abnormalities, which greatly facilitate their detection. Of the histologic criteria, the most significant are the irregularity in pattern, the anisocytosis and anisocaryosis and the crowding of the cells within each group.

In infectious processes, such as pulmonary tuberculosis and pneumonia, exfoliated cells may show atypical features but these are in no way comparable to those found in carcinoma cells. One condition in which exfoliated cells may appear in clusters

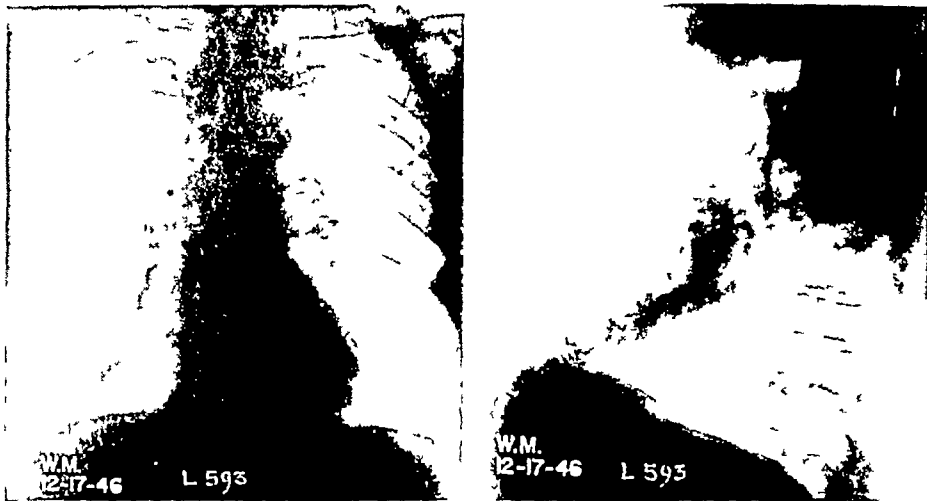


Figure 7 a and 7 b, Case L593. Photographs of x-ray plates showing infiltrative process in base of right lung.

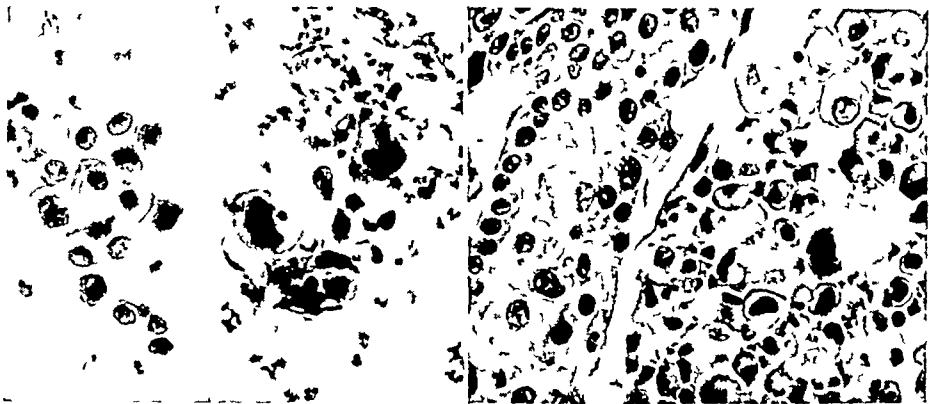


FIGURE 8

FIGURE 9

Figure 8, Case L593. Sputum smear. Cluster and group of malignant cells. Photomicrograph X285.—Figure 9, Case L593. Section of tumor of right lung showing bronchiogenic epidermoid carcinoma grade III. Note exfoliated cells on right half of section. Photomicrograph X285. (Courtesy of the Pathological Laboratory of Memorial Hospital)

suggestive of a neoplastic type of exfoliation is bronchiectasis. Because of such cell groups, false Class IV positive reports have been given in the first three cases of this type. We now feel that the atypical cells found in bronchiectasis can be differentiated from true malignant cells by the absence of nuclear abnormalities and by some distinctive structural characteristics. Oat cell carcinomas present a greater difficulty in diagnosis because of the smallness of the cells which may be easily overlooked unless found in sizable groups. Epithelial pearls when found in a sputum or an aspirated bronchial secretion always raise strong suspicion of a malignant neoplasm. Dense groups of lymphocytes are also highly suggestive. Thus far, we have noted such groups only in a small number of positive cases.

In the past three years, we have come to believe that the cytologic method is of definite value as an aid in diagnosing cancer of the lung. Evaluation of the advantages of this method to the clinician may be summarized as follows:

It helps in the diagnosis of obscure cases. In some instances where bronchoscopy and aspiration biopsy were negative and the x-ray examination inconclusive, a positive sputum report revealed the true nature of the lesion.

It aids in the earlier diagnosis of pulmonary neoplasm. At times, the sputum report has been positive from a day to weeks before any other histologic evidence of cancer was obtained. It is, therefore, of value for screening purposes in cancer detection clinics.

It tends to accelerate the diagnosis and to increase the percentage of operable cases. This is of particular importance since it enhances the chance of cure of these patients through surgical intervention. The poor results with x-ray therapy are only too well recognized. The gratifying results of early surgery are generally well appreciated.

It is particularly useful in establishing a diagnosis of carcinomas of the superior sulcus, so-called Pancoast's tumors. Tumors in this part of the lung are inaccessible to the bronchoscope. When x-ray findings are meagre, bronchial washings from both right and left main bronchi may decide the issue. Recently we had such a case in which the washing from the right main bronchus was positive (Class V) whereas the reading from the left was negative (Class I).

Because of its technical simplicity and low cost, repeated specimens can be obtained. This makes it particularly advantageous in postoperative and postirradiation follow-up.

### CONCLUSION

We wish to emphasize the difficulty in interpreting smears and the need of adequate training for laboratory men who wish to

undertake this type of work. The value of the method depends largely on the training and proficiency of the person interpreting the smears.

### CONCLUSION

Deseamos recalcar la dificultad de interpretar los frotos y la necesidad del entrenamiento adecuado de los médicos de laboratorio que deseen llevar a cabo esta clase de trabajo. El valor del método depende en gran parte del entrenamiento y la habilidad de la persona que interprete los frotos.

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## D I S C U S S I O N

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This is an important and timely subject, because carcinoma of the bronchus is unquestionably on the increase. Whether this is real or apparent is beside the point, there are more patients with carcinoma. Surgeons are treating it satisfactorily but the difficulty lies in getting patients to them early so that extirpation of carcinoma still can be done. Our attention was directed forcibly to this several years ago, when Dr. Herbut and I checked the cases of carcinoma of the bronchus that we had diagnosed by bronchoscopic biopsy and then checked to see how many the surgeon was able to treat. This number was small. Obviously there is something wrong. We felt that with the high percentage of positive bronchoscopic biopsies (reports in medical literature vary from 60 to 85 per cent), there should have been more for surgical treatment. The difficulty lay in the fact that a majority of patients are diagnosed too late and a positive bronchoscopic biopsy merely meant that the carcinoma was in a larger bronchus. We therefore concluded that something more should be done to aid in diagnosis particularly in those lesions which could not be visualized bronchoscopically, namely, upper lobe lesions and lesions

in the periphery of the lung which were beyond the view of the bronchologist. With the excellent work of Dr Papanicolaou in the diagnosis of uterine carcinoma we believed here was an opportunity since carcinoma of a bronchus is bronchogenic and cancer cells should be exfoliated and should appear in bronchial secretions. We started with a study of bronchial secretions of known bronchogenic carcinomas, and found that cancer cells appeared in variable numbers and could be identified.

Secretions are secured bronchoscopically from the bronchus that presumably is draining the lobe in which the roentgenogram reveals a shadow. Since there often is little or no sputum in early cases of carcinoma we were confronted with the problem of securing secretions bronchoscopically in one who had no increase in secretions. Various means were attempted but the majority of them were not satisfactory, and now we instil normal saline solution into the suspected bronchial subdivision, reaspirate the material and submit that to the laboratory for cytologic study. One often must employ posture, for example, with an upper lobe lesion the patient is placed on that side after the bronchoscope is inserted. With the aid of a curved aspirator for instillation of salt solution, about 2 or 3 cc are instilled and then reaspirated. Since that has been done our percentage of positive findings in lesions around the corner has increased.

It is of course important to pick up early lesions. Late diagnosis is inconsequential and only of didactic interest.

(Slides then were shown of five patients, all of whom had early pulmonary lesions with slight symptoms, roentgen findings that were only suggestive of neoplasm and negative bronchoscopic findings. Cytologic studies revealed carcinoma and all were treated surgically.)

In a recent study of our results which cover over 1,000 patients there were found 205 cases of carcinoma of the bronchus. Of these a positive bronchoscopic biopsy was secured in 76 (37.5 per cent), stenosis or deformity and fixation of a bronchus observed bronchoscopically in 46 (22.4 per cent), positive diagnosis by cytologic study of bronchoscopically removed secretion in 185 (90.2 per cent). This study therefore gave a 32.6 per cent margin of positive biopsies to the cytologic method in cases that were negative bronchoscopically. This group represents an important one for many of these represented early cases and amenable to surgical treatment.

I care not how you make diagnosis, the important thing is, make it early, do not wait until there are roentgen evidences of bronchial obstruction, copious sputum and palpable nodes and other evidences of advanced disease. We must make the diagnosis early. If you prefer to examine the sputum well and good. We

prefer bronchoscopy and believe the method of cytologic study of bronchoscopically removed secretion has contributed enormously at our clinic

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SEYMOUR M FARBER, M D , F C C P  
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I would like to mention a practical aid If a patient has sputum which is purulent or tenacious and loaded with bacteria it may be difficult to find malignant cells In a few of these patients we have given iodides and a week's course of penicillin Following the decrease in the amount of sputum and a change in its character we have been able to find malignant cells in a few patients Dr Cromwell's remarks concerning additional specific training for physicians and technicians must be stressed in this field It is well to keep in mind that there are courses in cytological diagnosis now being given in the different parts of the country

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#### *Closing Remarks*

*Henry A Cromwell, M D* After hearing these papers and discussions, I believe we all have a better idea of how to diagnose lung cancer earlier I feel that the use of this method inspires one to greater effort in cancer detection Dr Clerf brought out some pertinent facts and gave us some solid advice We owe him a debt of gratitude for his contribution to this meeting

It is a well known fact that treatment can only be as good as the diagnosis The first prerequisite to early diagnosis of cancer is to suspect its presence Early diagnosis is mandatory if one is to treat cancer with the idea of cure The delicate structure of the lungs prevents intensive irradiation therapy as is used in other parts of the body This leaves surgery the only sincere approach towards a cure Since Dr Evarts Graham performed the first pneumonectomy in 1933 great hope has been entertained regarding the treatment of this hitherto rather hopeless condition We do not have here a sure-fire single diagnostic procedure Rather, we have an added tool for use in diagnosis Dr Papanicolaou in his simple straight-forward manner has demonstrated what can be expected from the cytologic method of diagnosis and you have today seen the preliminary results The success or failure of this method depends on us as well as on the cytologist First it is up to us to suspect the presence of cancer and procure adequate specimens for smears, then follow up the results with good sound judgment

A lot more has to be learned about this work and many precautions have to be observed. One of these is that one should not depend on a single negative or positive report. Repeat specimens are urged. One cannot feel sure there is no cancer present just because the sputum, aspiration biopsy, or bronchial washing is negative. We have had cases in which at one time or another any one of these tests was negative, that is, none of them is always positive in the presence of cancer. Why a positive sputum obtains at times with a negative bronchial washing, or vice versa, is not clear. Cells may be exfoliating yet not be present in the specimen at a particular time. We do not know why this happens. It may occur because the smear is from the oral cavity and not from the bronchial tree. Statistics reveal that 10 per cent of lung cancers are potentially operable when first diagnosed. Only 60 per cent of these are likely to be surgically resectable. This is a low percentage. We are interested in trying to screen patients with early symptoms, particularly males. The percentage of bronchogenic carcinoma in the male is high—the literature states about 75 per cent. I think our series will run more nearly 90 per cent in males and 10 per cent in females. Here we have a little to work on as far as sex is concerned. Then there is the factor of age. We must watch males from say 40 to 55 years of age particularly. Below and above these ages cancer of the lung occurs in decreasing percentages.

Fixation and proper staining of slides are of prime importance. A pathologist may be extremely proficient but when it comes to sputum, or bronchial washings, or aspirates, he needs special training to fix and stain the smears and to recognize exfoliated cells.

By the use of the cytologic method we can expect earlier diagnoses and an increase in the number of cured cases by prompt surgical intervention.

# One Half Gram of Streptomycin in the Treatment of Pulmonary and Extrapulmonary Tuberculosis

## Report of 120 Cases\*

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Following the work of Schotz, Bugie and Waksman<sup>1</sup> on the discovery of the inhibitory effect of streptomycin on gram negative organisms, Feldman, Hinshaw and Mann<sup>2</sup> reported the marked suppressive effect of streptomycin on tuberculosis in guinea pigs Youmans and Carter<sup>3</sup> confirmed this by testing streptomycin on tuberculosis in mice

Keefer, Blake, Lockwood, Long, Marshall and Wood Jr,<sup>4</sup> in a review of the use of streptomycin in all types of infections in humans, reported the response of cases of tuberculous laryngitis, draining sinuses, osteomyelitis and the genito-urinary tracts Although the dosage was not clear, it appeared that over 1 gram daily was used Cook, Greene and Hinshaw<sup>5</sup> were encouraged with the use of streptomycin in the treatment of renal tuberculosis, as were Hinshaw, Feldman and Pfuetze<sup>6</sup> with pulmonary and extrapulmonary tuberculosis

Zenkel, Flippin, Nichols, Wiley and Rhoads,<sup>7</sup> using 0.5 gram dosages of streptomycin intramuscularly, found that the highest blood level was reached at 3 to 4 hours Anderson and Jewell<sup>8</sup> did not encounter toxic effects on 0.5 gram given every 3 to 4 hours, whereas Heilman, Heilman, Hinshaw, Nichols, and Herrell<sup>9</sup> showed that streptomycin could be given intramuscularly, intravenously, subcutaneously, intrathecally, orally and by nebulization with varying toxic results

With this background of literature and a few of our own preliminary cases, in March 1947 the staff of the Missouri State Sanatorium decided to initiate a series of cases using 0.5 gram daily with 0.25 gram injections at 12 hour intervals for 4 to 6 months Our plan was to compare results with those of investigators mentioned who had used a higher dosage Although our laboratory was not able to run sensitivity and blood levels, we

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believe as did Hinshaw<sup>10</sup> that the clinical test is the one test of prime importance. With the theory of subjecting the infection to a higher concentration of the drug the first few days, we divided one gram of streptomycin daily into 12 hour dosages for the first week and followed with the 0.5 gram schedule. One hundred twenty successive cases that had finished their courses and had been roentgenologically unchanged or progressively worse for the previous 3 to 6 months were chosen for this report. Their ages ranged from 8 to 75 years. Thirty-two cases were receiving either pneumoperitoneum or pneumothorax treatments. Of the 79 females and 41 males, 106 were caucasian and 14 were negroes. Ninety-one cases were classified as far advanced, 24 as moderately advanced and 5 as minimal according to the National Tuberculosis Association classification. The 5 minimal cases were treated because of either draining tuberculous sinuses or osteomyelitis. Several of the cases were terminal and several had fibrotic disease, but were treated for our own evaluation of streptomycin in this type of disease (Table I).

All but 6 patients had marked decrease of cough and expectoration and an increase in appetite. Of the 64 cases with an elevation of temperature, 31 had from 99 to 100° F, 15 from 100 to 101° and 18 above 101° F. Forty-three (67.2 per cent) returned to normal, 8 (12.4 per cent) returned to 99°, and 13 (20.4 per cent) had no change whatever (Table II). Ninety-nine cases could be evaluated as to weight. Those that did not gain weight even though of "normal" weight were classified in the "no-gain" or "lost-weight" column. Seventy (70.7 per cent) gained weight (1-5 lbs., 16.2 per cent, 5-10 lbs., 24.2 per cent, 10-20 lbs., 30.3 per cent), and 29 (29.3 per cent) had no change or lost weight.

*Laboratory Observation.* One hundred cases had abnormal sedimentation rates (Cutler method 2-10 mm per hour normal value). Twenty-six (26 per cent) returned to normal, 36 (36 per cent) decreased from 1 to 14 points although still above normal, and 38 (38 per cent) had no change (Table III). Eighty-seven cases were evaluated as to sputum conversion (by smear or concentrate). Thirty-nine (45 per cent) were converted, 3 (3.3 per cent) changed from consistently positive to alternately positive and negative, and 45 (51.7 per cent) remained positive. Several of the cases that had sputum conversion during streptomycin are now positive after the course was finished. One of the most interesting results first noticed was the cessation of hemorrhage or bloody sputum after the first few days treatment of streptomycin. Fisher, Fishburn and Wallace<sup>11</sup> reported that in 53 per cent of their cases hemoptysis disappeared.

*Exudative.* There were 36 cases of roentgenographic exudative



infiltration, 2 of which also had coexisting fibrotic disease. Ten cases were negroes. Nineteen cases were receiving either pneumoperitoneum or pneumothorax treatment with no response. Sixteen (44.4 per cent) had marked improvement or disappearance of the exudative infiltration in from 1 to 6 months. In 2 of these cases the collapse therapy may have been partially responsible. Seven (19.4 per cent) cases were moderately improved and 13 (36.2 per cent) had no improvement. Ten cases had converted sputums and 2 were changed from consistently positive to alternately negative and positive. Our results are not as favorable as the Veterans Administrations Groups (Table IV).

*Cavities* Thirty-two cases had roentgenographic cavities. Twelve (37.5 per cent) were healed or lost to view, 6 (18.8 per cent) were smaller, and 14 (43.7 per cent) were not improved or larger. Ten of the 12 healed cases were judged to have exudative infiltration before the course of streptomycin, and 2 of the 12 were judged to have a moderate amount of both exudative and fibrotic disease. There was no response to streptomycin in cavities of cases of fibrotic disease. In the "no-improvement" group, 7 had predominantly fibrotic disease, 6 exudative disease and 1 both types. All but 2 cases received streptomycin from 4 to 6 months. One of these received streptomycin for 61 days, had fibrotic type of disease and had no change, and 1 received streptomycin for 90 days, had exudative disease and had moderate decrease in the size of the cavity. Ten of the 12 "closed-cavity" cases were receiving pneumothorax or pneumoperitoneum treatments with no im-

TABLE I  
Age Range in Years

Age	8	15-19	20-29	30-39	40-59	60-75
No of Cases	3	10	43	30	11	120

TABLE II  
Clinical Results

		TEMPERATURE				WEIGHT	
		Total No	Total number decreased	Decreased to normal	Decreased to 99°	Total No	Gained
Mo State San	No	64	51	43	8	99	70
	%		79.6	67.2	12.4		70.7
V A <sup>4</sup>	No	160	117	76		223	188
	%		73.1	47.5			84.3

provement in the status of the cavity Twelve of the 32 cases having cavities had converted sputums, 3 of the converted cases still had cavities Nine of the "closed-cavity" cases had converted sputums Our results, as compared with the Veterans Group (Table V), are favorable

*Atelectasis* We have been impressed with the use of streptomycin in cases with atelectasis, especially if present in lungs receiving some type of collapse measures We believe that responses in those cases are probably due to dealing of endo-bronchial tuberculosis of the more distal bronchi Of the 5 cases studied, 3 cleared

TABLE III  
Laboratory Results

		SEDIMENTATION RATE			SPUTUM	
		Total No	Total number decreased	Decreased to normal 2-10 mm	Total No	Converted
Mo	No	100	62	26	87	39
State	%		62	26		45
San		184	94		190	82
V A <sup>4</sup>	%		51			43

TABLE IV  
Exudative Disease

		Total No	Improved marked or moderate	Marked improvement only	Minimal improvement or none
Mo	No	36	23	16	13
State	%		63.8	44.4	36.2
San		222	189		21
V A <sup>4</sup>	%		85		10

TABLE V  
Cavitation

		Total No	Healed or lost to view	Became smaller	No change or larger
Mo	No	32	12	6	14
State	%		37.5	18.8	43.7
San		182	47	67	68
V A <sup>4</sup>	%		26	37	37

completely, 1 improved, and 1 had no improvement. Canada reports that in 10 cases 8 had an increase of atelectasis.<sup>12</sup>

*Laryngeal-bronchial tuberculosis* This type of complication is always serious because of the slow response to local treatment, end results of stenosis with all its complications and the poor prognosis in many cases. Several of the cases were terminal, while others, in spite of positive sputum and bronchial tuberculosis, had stable x-ray findings with no evidence of active lesions. In many of these cases exhaustive study, including laminagraphs, revealed no "feeder" focus, and when the bronchial granulations healed, the patient's sputum became negative and remained so. There were 31 cases of laryngeal or bronchial tuberculosis. Only those cases having positive sputum and bronchoscopic evidence of granulations or ulcers of the larynx, trachea or bronchi were chosen. Seventeen (54.8 per cent) cases healed, 6 (19.35 per cent) improved, 6 (19.35 per cent) had no improvement, and 2 (6.5 per cent) had converted sputum but showed persistent granulation tissue. Of the 17 healed cases 9 had converted sputums. A few of the healed cases had single or bilateral cavities. The number of days of treatment ranged from 98 to 272. Lesions healed from 1 to 6 months after initiation of treatment, the average being about 3 to 4 months. Two of the "no-improvement" cases had had laryngeal tuberculosis from 6 months to 1 year and were terminal. These cases respond poorly to streptomycin although one case of 3 months duration, terminal with ulceration and partial sloughing of the epiglottis, and having massively enlarged bilateral cervical glands and extensive granulation of the pharynx and larynx, healed in 3 months. Eleven cases of the 31 had converted sputums. One case improved enough for pneumonectomy and a postpneumonectomy case healed ulcerations of the bronchial stump. Streptomycin is of the utmost benefit to those patients needing resection, but are delayed because of bronchial tuberculosis.

Our results do not seem to compare favorably with those on higher dosages, but perhaps the severity of some of our cases and their chronicity was an unfair test of the 0.5 gram dosage.

*Thoracic surgery* It is most difficult to evaluate the use of streptomycin used routinely in thoracoplasties and resections. Sixteen cases received streptomycin 1 week to 1 month before thoracoplasty and continued receiving the drug for 4 to 6 months. One was given streptomycin because of a bilateral spread of the disease after the first stage. The disease was promptly controlled and 2 more stages were carried out with resultant sputum conversion. Since none of the 15 cases had a spread of their tuberculosis during surgery, the use of streptomycin was probably unnecessary. Prevention of a spread cannot be credited to strep-

tomyacin since epidural anesthesia used routinely here results in almost no cause of spreads during thoracic surgery<sup>13</sup>

Of the 6 cases of pulmonary resection receiving streptomycin 1 to 3 months before surgery, each had tuberculosis with bronchiectasis for which resection was carried out. All patients were negative following surgery and none had spreads.

Five cases which we were packing daily with plain gauze had widely incised subcapular infections. Routine smears of the infection were negative for tuberculosis bacilli, nevertheless we feel the infections were definitely tuberculous. All cases except 1 healed, and all patients were of the opinion that there was a marked decrease in the amount of drainage and in their symptoms. One case with a pleural-cutaneous fistula did not heal, but this patient had had a draining subcapular infection for several years before sanatorium admission.

*Anal Fistula* Three cases having positive sputum had rectal or anal fistuli, which healed completely while taking streptomycin. One case was twice operated previous to streptomycin, but the internal fistulous opening could not be found. Curettments of the tract revealed tuberculous tissue. Drainage ceased in all cases in three days following initiation of streptomycin even though one case had had a fistula for 20 years.

*Draining Cervical Sinuses* Three cases with cervical sinuses were treated with streptomycin. All gave a history of drainage for over 1 year, and all healed during the course of the drug. One had recurrence after streptomycin was stopped. This patient, however, had extensive skin destruction of the upper one fourth of the anterior part of the chest which healed about 1 month after streptomycin was started.

*Bone* Five cases were treated for tuberculous osteomyelitis. Two had Pott's disease. 1 had tuberculous destruction of the knee joint with massive skin destruction, swelling and draining sinuses, and 2 had tuberculous osteomyelitis of the sternum. An interesting case was that of an 8 year old negro girl with symptoms and roentgenographic evidence of tuberculosis of the bones of both wrists, finger and a pericarditis with effusion. This patient actually receiving more than 0.5 gram in proportion to her size and age, had complete cessation of all symptoms in 3 months with roentgenographic evidence of healing of all bone lesions and disappearance of the pericarditis. One of the cases of Pott's disease had a surgical fusion at the time streptomycin was started and healed nicely. The other had had a fusion 4 years previously, but subsequently developed a large abscess in the right lumbar region with a fistulous tract extending upward and crossing the lower dorsal vertebrae to the bronchi of the medial basal segment of

the left lower lobe from where she constantly coughed and raised the pus. After incision of the abscess, she was given streptomycin intramuscularly and irrigations of the fistulous tract. All lesions healed and she became symptom free. The patient with the draining knee had skin grafting of the area of destruction with 100 per cent "take" of the graft even though the sinuses were still draining. The sinuses subsequently healed, fusion of the knee took place, and the patient is symptom free 9 months after discontinuance of streptomycin.

*Genito-Urinary* Eight cases were treated for tuberculosis of the genito-urinary tract. Three cases had tuberculous epididymi which were either draining at the time or were surgically removed with spillage of infected material into the wound. All healed by primary intention with the sinuses healing in 1 month and remaining healed. One case had a nephrectomy with primary wound healing. Five cases had positive urine with severe cystitis diagnosed by cystoscopy. Although streptomycin gave marked relief in 4 of the 5, none had converted urines. The case with no response had contraction of the bladder to 60 cc capacity. Cystoscopy in these cases revealed almost total healing of the severe cystitis. The reports of others are also discouraging regarding cures with higher dosages of streptomycin in tuberculosis of the kidney.<sup>4 5 10</sup>

*Intestinal* Seven had severe symptoms of intestinal tuberculosis, one of which was diagnosed by barium enema. All had symptomatic relief in 3 days to 1 month, with only one case having recurrence of symptoms after discontinuance of streptomycin.

*Bronchiectasis* Five positive sputum cases were treated for bronchiectasis diagnosed by bronchography. All had fibrotic disease. Basing our treatment on the probability of tuberculosis of the terminal bronchi, we found only 2 cases had conversion of sputum and none showed more than a minimal improvement in their x-ray films.

*Miscellaneous* One case with evidence of hematogenous spread of tuberculosis had tuberculous peritonitis diagnosed by laparotomy, lesions of the skin of the foot and finger and a subcutaneous abscess of the chest. All areas were proven tuberculous by guinea pig inoculation. In spite of the fact that the patient's x-ray film was negative, his sputum was positive by guinea pig inoculation. Nevertheless he responded excellently to streptomycin with complete alleviation of all symptoms and conversion of the sputum tested by the above mentioned method.

*Toxicity, sensitivity, blood levels* There was not a single case of toxicity in our series. Only 2 cases had evidence of sensitivity by developing a rash which disappeared in a few days during streptomycin treatment.

Unfortunately our laboratory was not equipped to carry out sensitivity tests and blood levels at the initiation of our studies. We are now carrying out a limited number of sensitivity tests and find that the bacteria are sensitive to 0.05 to 0.2 micrograms of streptomycin before treatment. Keefer, et al.,<sup>4</sup> report in their summary that 0.5 gram of streptomycin given intramuscularly results in blood levels of from 9 to 10 micrograms per cc. It seems reasonable, therefore, to assume that 0.5 gram dosage of streptomycin will have a bacteriostatic effect on the bacteria until resistance develops. There is a need for study to determine whether 0.5 gram daily dosages of streptomycin decreases or increases the period of formation of resistance of the tuberculous bacillus.

### *Discussion*

From the results of our studies it appears that there is need for further investigation with lower dosages of streptomycin given at longer intervals than has been the practice in the past. There is evidence that constant high blood levels of streptomycin are not required to counteract the tubercle bacillus as is the case with penicillin and gram positive organisms. Although the cases of extrapulmonary tuberculosis reported in this series are not numerous enough for statistical significance, the author believes from his experience with cases now being treated at the Missouri State Sanatorium that 0.5 gram daily dosage of streptomycin with injections of 0.25 gram at 12 hour intervals is adequate for good response in tuberculous cavities, enteritis, anal and cervical fistuli, draining sinuses, tuberculous epididymi, and sputum conversion. Tuberculous abscesses can now be incised and drained without the fear that the resultant sinuses will seldom heal. Exudative disease and laryngeal bronchial tuberculosis, if of recent origin and not too extensive, respond satisfactorily to our dosage schedule. If more extensive and of longer duration, a higher dosage (1 to 1.5 grams) should be used. Urinary tract tuberculosis appears to respond to 0.5 gram dosage as well as to the higher dosage since neither seems to cure permanently the disease.

Streptomycin has immeasurably improved the prognosis in negro patients who usually present the exudative type of disease. The often fatal spread following thoracic surgery can now be combated with marked encouragement. The condition of patients needing thoracic surgery, but whose lungs or bronchi are so severely involved by tuberculosis that surgery is contraindicated, can usually be improved enough that surgical collapse measures or resections can be carried out.

However, streptomycin should not be used as a substitute for proper collapse measures, nor should these measures be delayed too long with the hope that they will be unnecessary. In many instances the optimum time is lost while waiting for the end results of streptomycin treatment. Since 0.5 gram daily dosage of streptomycin appears to give no toxic effects, and since the toxic effects on the vestibular apparatus and auditory nerve are the most serious concern of those using high dosages, our studies are of particular value. Furthermore, I believe it worthy to investigate the development of resistance of the tubercle bacillus to streptomycin given in this lower daily dosage (0.5 gram) with injections of 0.25 gram at 12 hour intervals.

### SUMMARY

*Total number of cases* 120 pulmonary and extrapulmonary tuberculosis

*Dosage* 0.25 gram at 12 hour intervals

*Temperature* (64 cases) 67.2 per cent returned to normal, 12.4 per cent decreased to 99° F

*Weight* (99 cases) 70.7 per cent gained weight

*Sedimentation rate of the red blood cells* (100 cases) 62 per cent had a decrease

*Converted sputums* (87 cases) 45 per cent converted

*Exudative lesions* (36 cases) 63.8 per cent showed marked to moderate improvement roentgenographically

*Cavitation* (32 cases) 37.5 per cent were healed or lost to view, 18.8 per cent became smaller

*Laryngeal-bronchial tuberculosis* (31 cases) 54.8 per cent were healed, 19.3 per cent improved

*Toxicity* Not a single case was encountered in our series

Although there was not a sufficient number of the extrapulmonary and thoracic surgery cases for statistical significance, evidence is accumulating that good response occurs in draining sinuses of the rectum, anus, cervical and epididymi, spreads from thoracic surgery, osteomyelitis, and symptomatic relief in urinary tract tuberculosis.

### RESUMEN

*Numero total de casos* 120 casos de tuberculosis pulmonar y extrapulmonar

*Dosis* 0.25 gramo a intervalos de 12 horas

*Temperatura* (64 casos) 67.2 por ciento volvieron a lo normal, 12.4 por ciento bajaron a 99° F

*Peso* (99 casos) el 70.7 por ciento ganaron en peso

*Indice de sedimentacion de los eritrocitos* (100 casos) disminuyo en el 62 por ciento

*Espustos convertidos* (87 casos) se convirtio en el 45 por ciento

*Lesiones exudativas* (36 casos) el 63.8 por ciento demostro decidida o moderada mejoría en la roentgenografia

*Cavernas* (32 casos) el 37.5 por ciento se cicatrizaron o se perdieron de vista, el 18.8 por ciento disminuyeron de tamaño

*Tuberculosis laringeo-bronquial* (31 casos) el 54.8 por ciento se curaron, el 19.3 por ciento mejoraron

*Toxicidad* No se encontro ningun caso en nuestra serie

Aunque no hubo un numero suficiente de casos extrapulmonares o de cirugía torácica para que tuvieran significado estadístico, se estan acumulando pruebas de que ocurre una buena respuesta en fistulas con desague del recto, ano, ganglios cervicales y epidídimo, propagaciones consecutivas a cirugía torácica, osteomielitis, y alivio sintomático en tuberculosis del aparato urinario

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# Streptomycin in Tuberculosis of the Larynx\*

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Most of the previously reported work on streptomycin therapy has utilized doses of the drug varying from one to three grams a day. The group of laryngeal cases reported here has been on doses far lower than the therapeutic doses generally accepted today. Streptomycin in doses of one to three grams a day produces a high incidence of toxic reactions, and this study of clinical material was undertaken with the express purpose of determining whether or not streptomycin in small doses, would prove to be of therapeutic value. The latest recommendations of the American Trudeau Society and the Veterans Administration are for a daily dose of streptomycin of about one gram for most cases of pulmonary tuberculosis and its extrapulmonary complications. In our series of cases we used both smaller doses and intermittent therapy, namely, 0.1 gram daily, 0.2 gram daily, 0.5 gram daily and 1 gram of streptomycin once weekly.

Tuberculosis of the larynx was chosen for this study because it offers a fairly accessible organ for direct and frequent observation. The same observer recorded findings in all of these cases, and only severe or moderately severe cases were chosen for treatment in order to provide sufficient gross pathologic findings to enable the observer to appreciate changes in the appearance of the larynx over a brief period. Laryngeal lesions have previously been reported as highly susceptible to improvement by streptomycin in the usual 1-2 gram daily dose, from 75-90 per cent of the cases.

Twenty-six cases were treated and observed over a period of three months. All twenty-six cases had far advanced pulmonary tuberculosis as well as laryngeal involvement and all had recent positive sputa for the tubercle bacillus. Five cases were given only 0.1 gram daily, 8 received 0.2 gram daily, 5 received 0.5 gram daily and 8 received 1.0 gram once a week. Each dose was administered intramuscularly, in a single injection daily or weekly over a period of three months.

The 5 cases receiving 0.1 gram daily were considered controls, as originally little therapeutic effect was expected and because the total of cases would have been appreciably reduced by following

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non-treatment controls One showed slight improvement, three showed no improvement, and one case was much worse One of the cases which did not improve required a tracheotomy because of a fixation of the vocal cords in the mid-line Two of these five cases had previously been treated with large doses of streptomycin for tuberculous laryngitis and had been reported as healed, but the tuberculosis of the larynx recurred and they were included in this group

The eight cases given 0.2 gram of streptomycin daily presented an entirely different picture One showed no change, one improved slightly, one improved moderately, and the remaining five cases improved very markedly These cases could not be considered healed, by mirror examination, but after three months of 0.2 gram of streptomycin a day, all had changed from moderately severe and severe cases of tuberculous laryngitis to mild or inactive cases Two of the cases who had severe dysphagia, or pain on swallowing, were completely free of pain after 5 to 10 days respectively One patient had a severe tuberculous laryngitis with obstructive symptoms, but after three months had a normal airway and her general improvement was marked by a weight increase of 35 pounds The only case which showed no improvement was one which had previously improved under streptomycin therapy for tuberculous laryngitis and which had recurred

Four of the five cases given 0.5 gram daily improved and one showed no improvement Of the four improvements, one was slight, one moderate and two marked Two cases with pain on swallowing cleared completely in 5 days to 2 weeks

The last group of 8 cases received 1.0 gram of streptomycin only once a week After three months, 6 of the 8 presented improvement, one mild, one moderate and four cases of very marked improvement One case, presenting dysphagia, lost all symptoms of pain on swallowing after the second weekly dose

On analyzing this series of 26 cases we find that percentage of improvement with small doses, 0.2 gram daily, 75 per cent, 0.5 gram daily, 80 per cent, and 1 gram weekly, 62 per cent, compares very favorable with the percentages of cases improving on 1-2 grams daily, i.e., about 70 per cent in all cases This high percentage of improvement in laryngeal tuberculosis on doses of 0.2 gram daily, 75 per cent, as compared to no improvement under a course of 0.1 gram daily, implies a much lower limit of therapeutic effect than is ordinarily accepted and could be studied further The cost of the drug is reduced considerably and the annoyance to the patient of several daily injections is lessened

Five cases presented pain on swallowing All five improved considerably in a short time and obviated the necessity of procedures

such as electrocautery, superior laryngeal nerve block or section and the use of anesthetic sprays. This one feature of streptomycin therapy in tuberculosis of the larynx has been universally noted.

Reports of a high percentage of cures with streptomycin in tuberculosis of the larynx may be misleading, however, if no mention is made of the condition of the larynx at a later date, after the cessation of streptomycin therapy. Several of the cases reported in this series had previously been reported as streptomycin cures, but the laryngitis recurred. In the series of 26 cases reported here, especially in the cases noted as clinically improved at the cessation of 3 months of therapy, several recurrences have already been observed, and continued observation of the remaining cases will doubtlessly uncover more. The improvement is temporary in many cases. Permanent cure depends on arrest of the pulmonary process.

The main toxic effect of streptomycin has been on the vestibular apparatus. Deafness is rare, but vestibular dysfunction occurs in the majority of the cases treated with 2 grams daily, and less frequently with 1 gram daily. In this series there were no complaints of deafness, and only one individual complained of dizziness, but the caloric responses here were normal. Toxicity to smaller doses, 0.5 gram and less, as used here, is apparently insignificant.

As for resistance of the tubercle bacillus to the streptomycin, it is conceivable that smaller doses will have the same end-result as larger doses. These 26 cases were examined for evidence of resistance at the onset of treatment, but the presence or absence of resistance at the conclusion of the therapy has not been determined as yet, for most of the cases recently completed the therapy. Four of the twenty-six cases had previous streptomycin therapy for tuberculous laryngitis. None of these showed any appreciable improvement in this series and studies of the tubercle bacilli showed that a resistance had developed after the first or during the second course of therapy. The twenty-two cases without previous streptomycin therapy had susceptible or sensitive bacilli. However, at the conclusion of the therapy of 0.2 and 0.5 gram daily, we have already shown a well marked resistance in five cases, and the laboratory work on the other cases has not been completed as yet.

### CONCLUSIONS

- 1) Small and intermittent doses of streptomycin down to 0.2 gram daily, will give the same clinical improvement in cases of laryngeal tuberculosis as larger doses, and will especially relieve the severe pain as in the larger doses.

2) A large percentage of recurrences of the disease may occur no matter what dose is used originally

3) Toxicity is negligible with the smaller and intermittent doses, but the tubercle bacilli develop a resistance to small doses just as they do toward larger doses of streptomycin

### CONCLUSIONES

1) Las dosis pequeñas e intermitentes de estreptomícina hasta de 0.2 gramo al día, da la misma mejoría clínica en casos de tuberculosis laringea que las dosis mas grandes y especialmente alivia el dolor severo lo mismo que las dosis mas grandes

2) Puede ocurrir un alto porcentaje de recidivas de la enfermedad, no importa cual sea la dosis empleada al principio

3) La toxicidad con las dosis pequeñas e intermitentes es insignificante, pero el bacilo tuberculoso desarrolla resistencia a las dosis pequeñas en la misma manera en que la desarrolla con las dosis mas grandes de estreptomícina

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# Aerosol Antibiotic Therapy in Suppurative Diseases of the Lung and Bronchi\*

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Inhalation therapy has become very popular both with physicians and the laity. While the use of antibiotics by nebulization is rather recent, the utilization of germicidal mists and therapeutic gases dates back many years. Those interested in a complete review of the historical background for aerosol therapy should read Segal's excellent article on the subject.<sup>1</sup>

The original report on penicillin aerosolization was made by Bryson and his associates<sup>2</sup> in 1944 and was an outgrowth of their work on the physical and biologic properties of aerosol for the Technical Division, office of the Chief, Chemical Warfare Service. Since then, stimulated by their findings, clinicians have made exhaustive trials with this method in pulmonary infection not only with penicillin but also with the sulfonamides, the sulfones and more recently with streptomycin.

While this report is limited to the results obtained in suppurative diseases of the lungs and bronchi by penicillin and streptomycin aerosolization, it should be noted that infectious asthma, pneumonia, laryngotracheobronchitis and pulmonary emphysema associated with infectious bronchitis or bronchiectasis were also thus treated. However, as is the case with reports of others, the number of patients in the latter group is too small to warrant final evaluation.

When one realizes the extensiveness of the inner surface of the lungs there is little wonder that effects similar to that of intravenous injection can be obtained by inhalation. In fact both Bryson<sup>3</sup> and Barach<sup>4,5</sup> and their associates have demonstrated in the experimental animal and in humans that a more uniform blood level of penicillin can be maintained by the inhalation method than by intermittent intravenous or intramuscular injections. Levine<sup>6</sup> has gone even further and has satisfied himself that aerosol penicillin will effect improvement in bronchiectasis when other methods fail.

That aerosolized materials when inhaled penetrate the outer-

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most air sacs of the lungs and are uniformly distributed was demonstrated by Krueger, et al,<sup>7</sup> using India ink and radioactive chromic phosphate as indicators. High local or topical concentrations are thus made possible.

The detection of penicillin in the blood and urine after administration of penicillin aerosol is proof of its absorption. However, it does not follow that the blood level necessarily is a measure of its topical effectiveness. It has been shown that satisfactory clinical results can be obtained with low and even no penicillin levels. It is for this reason that Segal<sup>8</sup> and his associates feel that the determination of blood levels is more of academic interest than of practical value. The clinical course is a better criterion of the local effectiveness of penicillin aerosol. Besides, factors other than alveolar absorption determine blood levels. These as listed by Segal<sup>9</sup> are the equipment used, the dosage and types of penicillin given, the absorption variations of accumulated pus and secretion and the technic of determining blood levels.

More recently Bryson<sup>10</sup> has shown that the bacteriostatic effect of penicillin and streptomycin aerosol can be enhanced by using



FIGURE 1 Method of Aerosolization

a detergent as the solvent for the drugs. Detergents or wetting agents have the properties of emulsification and of reducing surface tension. These properties serve to break up pus and cellular detritus and in this manner assure better contact between micro-organisms and the antibiotic. Already the combination of penicillin with detergent solutions has resulted in reduction of mortality in mice with experimental pulmonary disease as compared with a control series treated with penicillin aerosol alone. Clinical trials are being made and while a final report cannot be given at this time, results indicate that wetting agents likely will play an important role as adjuncts to simple aerosol therapy.

Intrabronchial instillation of penicillin or streptomycin has proved of additional value in some instances in which aerosol therapy was used and according to Siltzbach<sup>11</sup> better results than with aerosolization can generally be obtained. The method involves inconvenience to the patient and in my experience is seldom necessary. Furthermore, the use of this method does not obviate the interference offered by pus for contact of the drug with the micro-organisms. I believe that wider use of detergents will increase the efficacy of aerosol therapy without necessitating bronchoscopic or tube intubation instillation of antibiotics.

It has been long recognized that a knowledge of the bacterial content in suppurative pulmonary disease is not of real importance



FIGURE 2 Microscopic section of a dilated bronchus of an excised lobe untreated prior to operation. Note pus and cellular debris within bronchial lumen.

The introduction of penicillin and particularly streptomycin has changed the picture since it is considered essential to know whether one is dealing with sensitive or resistant organisms. This information is especially valuable if the benefits of multiple antibiotic



FIGURE 3 Microscopic section of a dilated bronchus of an excised lobe treated with penicillin aerosol prior to surgery. Note clear bronchial lumen.

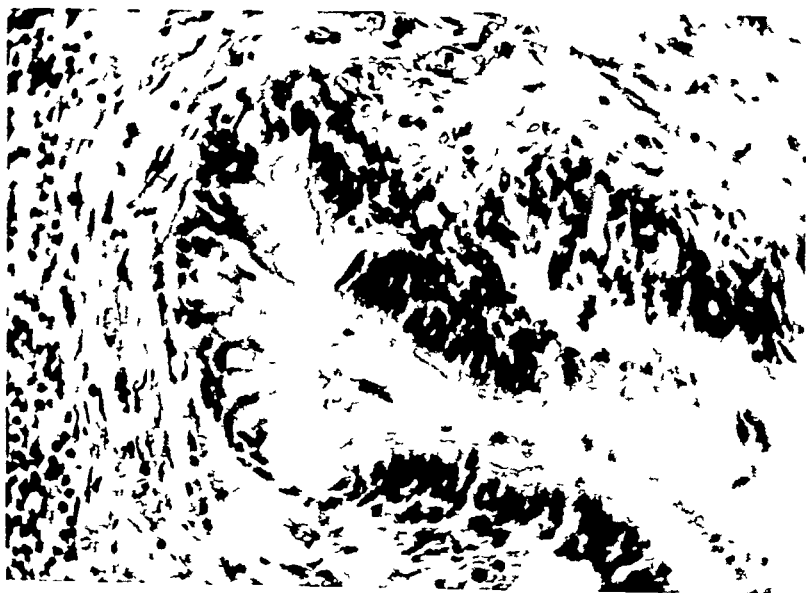


FIGURE 4 Same as figure three—high power view.





FIGURE 5

FIGURE 6

FIGURE 7

*Figure 5* White female, aged 32 years, admitted with cough and expectoration of foul sputum. Symptoms of 13 years duration. After 3 weeks of penicillin aerosol cough and sputum ceased. Bronchogram shows sacular bronchiectasis of the left lower lobe.—*Figure 6* Same patient, oblique projection showing sacular dilatations.—*Figure 7* Same patient after left lower lobe lobectomy. Residual lipiodol shadows are seen in the right lower lobe. Symptom free.

therapy is sought. Yet, despite what has just been said, I feel that aerosol therapy can be properly carried out without facilities for such determinations. It is nice to have them but from a practical point of view the clinical course is a good therapeutic guide. Our own and the experience of others indicate that the vast majority of patients who respond favorably to antibiotic aerosol therapy do so to penicillin alone.

The response to aerosol therapy is rapid and decisive, in fact in some instances it is dramatic. Fever and toxicity subside, the amount of daily sputum is diminished and in many cases secretions are entirely abolished, if the character of the sputum is foul, the odor is lost, serial roentgenograms of the chest reveal partial to complete resorption of the perifocal infiltrates and gross and microscopic sections of excised lungs show dilated but clean bronchi in contrast to bronchi filled with cellular debris and pus in untreated lungs or in cases which fail to respond to treatment. Those who have followed their cases with bacteriological studies have been impressed with the disappearance of susceptible micro-organisms.

If the above effects of antibiotics were permanent, the management of respiratory disease would indeed be simple. Unfortunately, this is not the case. In suppurative bronchiectasis the best results are obtained in the surgical cases in which penicillin and/or streptomycin aerosol seems to improve the surgical risk for the patient. He comes to the operating table either symptom-free or with minimal cough and expectoration. It is a general observation that thus prepared the patient is anesthetized with little or no difficulty and maintains the anesthetic state for many hours without ill effects and postoperative complications such as pneumonia and atelectasis are minimized.

In the non-surgical cases, the effects of penicillin and streptomycin are temporary and in most instances recurrences take place. But even these patients may sustain their attained improvement for months or longer and if symptoms do return, may again benefit by re-institution of aerosol therapy. In some, supplementary deep x-ray therapy may give more permanent results.

Prior to the introduction of the antibiotics, early incision and drainage was considered urgent in the proper management of acute lung abscess. Amelioration of symptoms such as fever, toxicity, cough and expectoration and obliteration of the abscess cavity followed in only about 15 per cent without surgical intervention. The use of penicillin singly or in combination with streptomycin has reversed the picture in so far as symptomatic relief is concerned. The follow up of "cured" cases has not been sufficiently long to determine whether spontaneous obliteration of

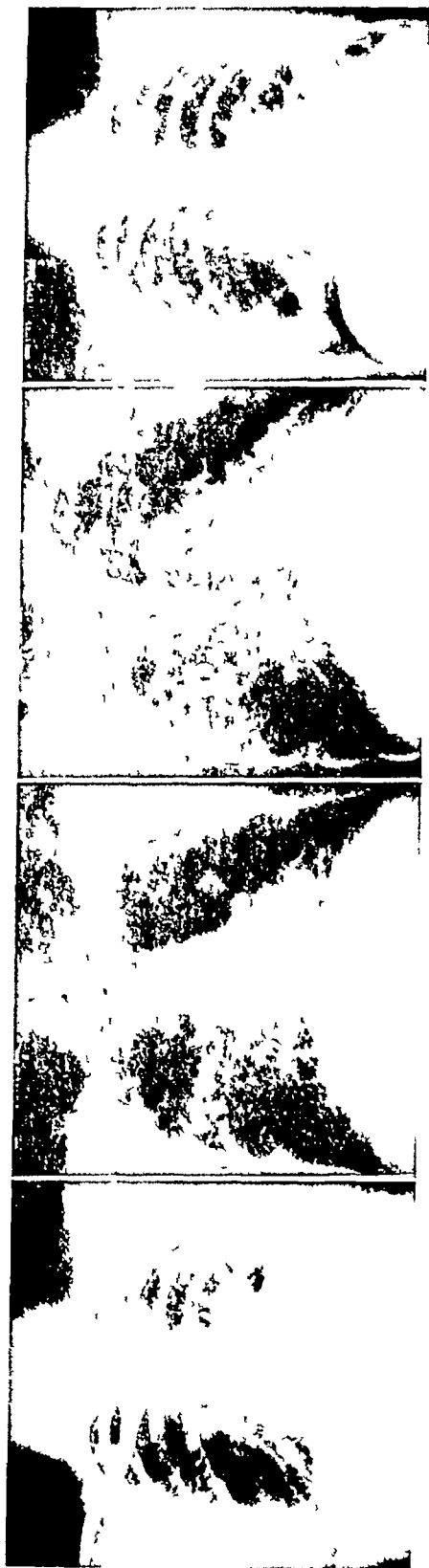


FIGURE 8

FIGURE 9

FIGURE 10

FIGURE 11

*Figure 8* White male, aged 43 years, admitted with cough, expectoration of purulent sputum, and history of repeated hemoptyses. Roentgenogram shows broncho-pneumonia left lower half of lung field and multiple ring shadows in right mid lung region. Duration of symptoms since childhood—*Figure 9* Same patient after one month of penicillin aerosol. Occasional cough not productive of sputum. Bronchogram shows cystic bronchiectasis of both lungs—*Figure 10* Same patient, oblique view—*Figure 11* Same patient. Roentgenogram shows residual lipiodol shadows. Note almost complete resolution of pneumonia in left lung. Symptom free for past ten months.

abscess cavities has been materially increased above the figure given

One thing is clear, surgery is no longer an immediate issue and when it does become necessary the patient is usually a much better candidate than was the case prior to antibiotic therapy. Moreover, the tendency now is to favor excision of the involved segment of the lung rather than pneumonostomy as it is believed that in many cases dilatation of the radicles of the bronchus draining the abscess cavity exists either at the time the lesion is discovered or develops later. As in bronchiectasis so in lung abscess, the preoperative preparation of the patient can be made more ideal and postoperative complications minimized by aerosol therapy.

Toxic effects such as sore tongue or stomatitis, edema of the lips or mucosa of the mouth, generalized urticaria and dyspnea have been reported. In the series of cases herein presented, sore tongue was encountered twice and dyspnea in two other instances, the latter in the group comprising infectious asthma and fibrosis with emphysema. Stomatitis is readily controlled by proper oral and dental hygiene and rinsing of the mouth with warm saline solution at the completion of each treatment. The allergic reactions mentioned above are easily managed by any of the antihistamine drugs. If dyspnea develops, discontinuing the drug brings about early relief. Subsequent re-institution of inhalations may not bring about return of the complaint. In one case, however,

LUNG ABSCESS		
	Type of Surgery	Results
SURGICAL SIX CASES	PNEUMONOSTOMY 1 case	Well
	PNEUMOSTOMY + lobectomy 2 cases	Well
	LOBECTOMY 3 cases	Well
	2 patients improved and awaiting surgery	
NON-SURGICAL FOUR CASES	2 patients obtained spontaneous closure of abscess cavity. In one, cavity has remained closed two years, in the other, recent recurrence has taken place after 6 months of closure. Latter patient awaiting surgery.	

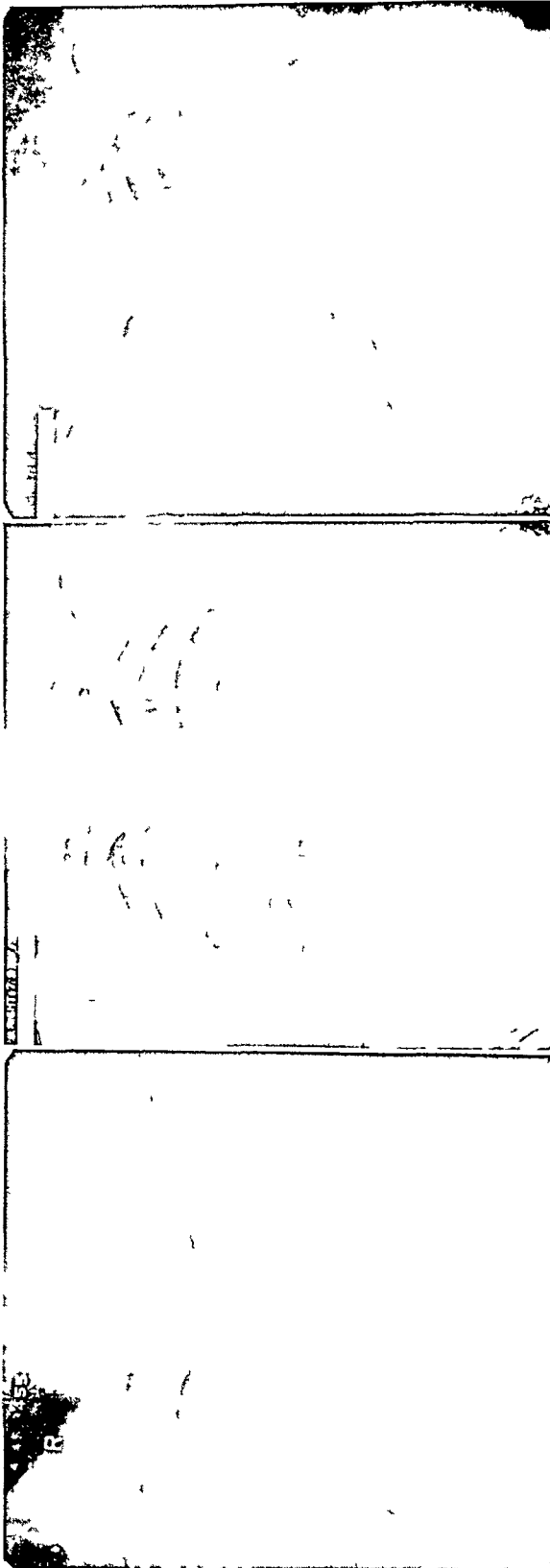


FIGURE 12

FIGURE 13

FIGURE 14

*Figure 12* White diabetic female, aged 53 years. Admitted from another hospital with cough and expectoration of foul sputum. Despite parenteral penicillin and sulfa therapy for 2 months prior to admission, improvement failed to take place. Roentgenogram shows a large abscess cavity in the left upper lobe—*Figure 13*. Same patient after 10 weeks of penicillin aerosol therapy. Note disappearance of cavity leaving residual infiltrate. Symptoms minimal at this time—*Figure 14*. Same patient after four months of aerosol therapy. Note complete resolution of residual infiltrate shown in *figure 13*. Symptom free.

the aerosol therapy had to be discontinued permanently because dyspnea returned each time aerosolization was re-established

Various methods of nebulization are in use. The fundamental principle is that the nebulizer be so constructed as to emit small particles, 5 microns in diameter or less, if penetration of the



FIGURE 15



FIGURE 16

Figure 15 Same patient Bronchogram showing absence of bronchiectasis—

Figure 16 Same patient 1 year after discharge. Note absence of any abnormal change in the left lung. Has been symptom free since discharge

### BRONCHIECTASIS

	Pneumonectomy	Lobectomy	Lobectomy plus Lingulectomy
<b>SURGICAL</b>			
18	6	9*	3
<b>CASES</b>			

\*One patient had right middle and lower lobes excised

	Symptoms Abated	Symptoms Reduced	Recurrences
<b>NON-</b>			
<b>SURGICAL</b>	3*	15**	In 3 instances all derived from "Symptoms Reduced" group In each instance severity and character of symptoms as existed prior to aerosol therapy, returned. Two have responded favorably to re-institution of previous therapy
18			
<b>CASES</b>			

\*Only 6 months Follow-up

\*\*Followed from 3 months to 2 years

smallest bronchioles and the alveoli is to be expected. Larger particles are impinged by convection in the nose, throat and upper respiratory passages and are undesirable. Nebulization is generally accomplished by employing a stream of oxygen from a high pressure cylinder to a serviceable nebulizer. In the beginning of our work a Y tube was attached to the rubber connection between the regulator of the oxygen tank and the nebulizer. During inspiration the open end was closed by a finger which was released during expiration resulting in the escape of oxygen during this phase of respiration. More recently the Y tube has been replaced by a demand valve which saves the oxygen that used to be lost in the expiratory phase. To minimize the loss of the antibiotic during expiration a rebreathing bag is attached to the nebulizer. A flow of 6-10 liters per minute of oxygen may be employed. Either normal saline or distilled water is used as the diluent.

Patients too ill to cooperate with the demand valve arrangement described above, may be given penicillin or streptomycin either parenterally for several days when sufficient improvement takes place to switch to aerosol or through an oronasal meter mask by attaching the nebulizer to the latter. Patients with dyspnea and/or cyanosis who require oxygen in addition to aerosol therapy may be given both through a head tent. This method is particularly useful in children. Prigal<sup>12-14</sup> described a combined steam generator and aerosolizer which produces a warm moist aerosol capable of giving high therapeutic blood levels of penicillin. He claims it is more economical to operate and the small size makes it convenient for use at home, in the office, or in the hospital.

The results in 36 cases of bronchiectasis and in 10 of lung abscess are tabulated below. No further explanatory remarks are necessary except to stress that the figures amply support the statements made above regarding the clinical and anatomical effects of aerosol therapy in bronchopulmonary suppuration. Finally, it is to be noted that in only three instances was penicillin supplemented by streptomycin.

Since the paper was submitted for publication, we have utilized a small bedside or table pump for nebulization instead of oxygen pumps. By a number of manufacturers are now on the market at very reasonable cost. For patients who have obtained the initial improvement hand bulb nebulizers which produce a fine mist are now available for continued therapy at home.

### SUMMARY

1) The results in 46 cases of bronchopulmonary suppuration treated by aerosolized antibiotics are reported.

2) Methods of nebulization are briefly reviewed

3) It is stressed that the local concentration and the topical effectiveness of the antibiotics judged by the clinical and anatomical course of the disease are more important criteria than the blood level

4) Penicillin and/or streptomycin aerosol therapy usually brings about appreciable clinical and anatomical improvement and therapy minimizes the operative risk in patients able to meet requirements for excisional surgery

5) In non-operative cases of bronchiectasis attained improvement may be maintained for months or longer although recurrences are frequent Favorable responses to aerosolization may be repeatedly obtained

6) With the use of antibiotics surgical drainage is no longer an emergency in lung abscess Because bronchiectasis not infrequently complicates lung abscess, extirpation of the involved lung segment is favored

7) Whether the number of lung abscesses which heal spontaneously has increased cannot be stated unequivocally at this moment

8) Antibiotics by nebulization are more convenient for the patient and their effectiveness equal, and in some instances more definite, than parenteral administration

## RESUMEN

1) Se informa sobre los resultados obtenidos en 46 casos de supuración broncopulmonar tratados con aerosoles de antibióticos

2) Se repasan brevemente los métodos de nebulización

3) Se recalca que la concentración local y la eficacia tópicos de los antibióticos, a juzgar por la evolución clínica y anatómica de la enfermedad, son criterios más importantes que el nivel sanguíneo

4) El tratamiento con aerosoles de penicilina o estreptomicina, o de ambas drogas, generalmente causa apreciable mejoría clínica y anatómica y reduce al mínimo el riesgo operatorio en pacientes que satisfacen los requisitos para la cirugía de excisión

5) En casos de bronquiectasia que no pueden ser operados es posible mantener la mejoría obtenida por periodos de meses o más, aunque son frecuentes las recaídas Pueden obtenerse repetidamente las respuestas favorables a la terapia con aerosoles

6) Gracias al uso de antibióticos, la canalización quirúrgica ya no es una emergencia en el absceso pulmonar Como quiera que con bastante frecuencia complica la bronquiectasia al absceso pulmonar, se favorece la extirpación del segmento pulmonar invadido

7) Al presente no se puede declarar en forma inequívoca si ha



aumentado el numero de abscesos pulmonares que se cicatrizan espontaneamente

8) La administración de antibióticos nebulizados es de mas conveniencia al paciente y su eficacia iguala, y en algunos casos supera, a la administración parenteral

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Nebulization therapy is effective in providing at least temporary reduction of pulmonary secretion in most patients who have non-surgical bronchiectasis Primary bronchial dilatation is not affected The patients are still subject to the hazards of a deformed bronchial tree It is strongly recommended that they continue therapy at home

In asthma caused by susceptible micro-organisms, aerosol penicillin and/or streptomycin are indicated whether the chronic or

the acute active stage is encountered Four daily sessions with antecedent use of one-fourth to one-half per cent neosynephrine and a solution containing 100,000 units of penicillin or/and 0.025 grams of streptomycin with eight liters of oxygen, and followed by one or two cc of normal saline are used The results are almost unbelievable, among our 23 cases of infectious asthma seen during the last 15 months 16 were completely relieved and three others were materially aided

Krasno, L, Karp, M and Rhoads, M S ("The Inhalation of Dust Penicillin," *Annals of Int Med*, 28 607-608, March 1948), have described a mask for home and office use This mobilizes penicillin dust with a resultant marked diminution of bacterial flora, improvement in signs and symptoms, and an effective blood level We are in the process of investigating this as an adjuvant therapy in tuberculosis, after the maximal benefit has been reached via parenteral administration

#### *Reactions to Penicillin in Aerosol*

Several reactions have occurred Two with mild generalized erythema three with localized irritation about the mouth and tongue with soreness, dryness and some edema One patient had sternal discomfort, which was abated with oral anti-histamines

Penicillin or streptomycin or both via inhalation are not cures, but a valuable adjunct in treating bacterial conditions of the upper and lower respiratory tract

Allergic reactions to penicillin may occur with any method of administration No cases of vertigo, arthralgia or eighth nerve involvement occurred in our streptomycin treated cases by nebulization

One should not depend completely on penicillin inhalations where complete control is not available, i.e., the aged, in the home, and where bacteremia may exist

Mechanical obstructions in the respiratory tract, even with the use of detergents, reduce the efficaciousness of the method

Recurrences following discontinuation of therapy in chronic non-surgical disease were common

Until we have available a method of introducing effective antibiotic therapy in acute and chronic respiratory diseases, easily administered—without the high cost of oxygen, the tediousness of administration and close supervision—aerosols should be limited to hospital and office use, and only the occasional patient at home One injection of procaine penicillin is much less trouble than a minimum of 80 minutes of supervised nebulization

# Bronchogenic Carcinoma\*

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During the past eleven years from 1937 to 1948, 50 cases of primary lung tumor were observed at Murdale Sanatorium. Three of these cases were bronchial adenoma, although they are considered as potentially malignant, they will not be included in this presentation. There remain 47 cases of primary bronchogenic carcinoma for consideration. The majority of these cases had been diagnosed as pulmonary tuberculosis prior to admission and a few were sent in for observation and diagnosis. Only two patients had both tuberculosis and bronchogenic carcinoma. Five of the 47 patients with bronchogenic carcinoma were treated for a number of months at home as cases of pulmonary tuberculosis. All entered Murdale Sanatorium later with inoperable lesions although two had apparently operable lesions when first seen by their physicians.

That the two diseases may simulate one another is well known, but there are sufficient differential diagnostic points to enable one to make a diagnosis without too much difficulty or delay. In both diseases early diagnosis is stressed, because the prognosis is directly proportional to the stage of the disease. In far advanced tuberculosis, many patients can be saved, but in advanced bronchogenic carcinoma the prognosis is hopeless.

Of the 47 cases, 35 were proved: 17 by postmortem examination, 17 by biopsy, and one by the presence of tumor cells in the pleural fluid. The remaining twelve cases were diagnosed on the basis of clinical, roentgenologic and bronchoscopic findings. Four of these twelve cases had rib metastases, and one had paralysis of the right hemidiaphragm and vocal cord.

## *Incidence, Age, Sex and Race*

There has been considerable discussion during the past thirty years as to whether the increase in primary bronchogenic carcinoma is apparent or actual. The matter is a controversial one. We merely wish to express the opinion that the reported increase

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is relative rather than absolute. We attribute the apparent increase to improved diagnostic methods, such as greater use of radiologic procedures, the bronchoscope and a better concept of the pathology of lung tumors. We are cognizant of the fact that with an increase in longevity, people have more of an opportunity to die from malignancy than in the younger age groups.

Primary bronchogenic carcinoma is now second only to carcinoma of the stomach as a cause of cancer death. At postmortem examination it is found in slightly over one per cent of all necropsies and comprises 10 per cent of all carcinoma found at postmortem examination.

Primary bronchogenic carcinoma may occur at any age, but there are surprisingly few cases reported under 40 years. Bjork<sup>1</sup> in an analysis of 345 cases from the Brompton Hospital for diseases of the chest in London, reports 87.8 per cent of the cases were 40 years and older. The average age of our patients was 55.4 years. Fourteen were between the ages of 40 to 50, twenty-two were between 50 and 60 years, and eleven were over 60 years. The youngest patient was 40, and the oldest was 73 years old.

Thirty-five of our patients were males and 12 were females, giving a ratio of three to one. In a larger series of cases reviewed by Bjork,<sup>1</sup> Ochsner and his associates,<sup>2</sup> and others, approximately 90 per cent were males. All of our cases were white, but according to Ochsner and his associates<sup>2</sup> the ratio between negro and white is two to one in favor of the white race.

### *Etiology*

The cause of bronchogenic carcinoma is not known. There have been numerous reports suggesting chronic pulmonary irritation as an etiologic factor. As yet there has been no proved relationship between bronchogenic carcinoma and the numerous causes of chronic pulmonary irritation.<sup>3</sup> Two patients were molders who had roentgenologic evidence of silicosis, one proved on necropsy to have both diseases. Three other cases had considerable foundry dust exposure with questionable silicosis, as indicated by the roentgenogram, but no postmortem examination was permitted in these cases.

### *Pathology*

It is now generally agreed that bronchogenic carcinoma arises from an undifferentiated stem cell in the basal membrane of the bronchus. Grossly, the right lung is more frequently involved than the left lung. From roentgenologic and postmortem findings in our cases, the right lung was the site of the primary lesion in 23 cases and left lung in 18 cases. In the remaining six cases the

primary site could not be determined Ochsner and his associates,<sup>4</sup> in an analysis of 4732 cases collected from the literature, found that 58.3 per cent of the tumors were in the right lung and 41.7 per cent in the left lung. The upper lobes are more frequently involved than the lower lobes. The tumors are primarily hilar in location, arising in the majority of cases from the main stem bronchi or the secondary, lobar bronchi.

Microscopically bronchogenic carcinoma is classified into three types.\* Squamous cell carcinoma is the most frequent. It offers the best prognosis as it grows slowly and metastasizes late. Undifferentiated cell type is slightly less frequent than the former, and adenocarcinoma, the third type, occurs in approximately 20 per cent of all the cases. Both the undifferentiated and adenocarcinoma are more rapid in their progress, metastasizing early with a correspondingly poor prognosis.

Bronchogenic carcinoma is noted for its widespread metastases. Ochsner and DeBakey,<sup>5</sup> in an excellent article, review the incidence and site of metastasis in 3047 cases collected from the literature. The regional lymph nodes are most frequently involved, an incidence of 72.7 per cent. From a surgical standpoint the involvement of the regional lymph nodes is considered to be 100 per cent, and they are resected if possible. Of diagnostic importance are the supraclavicular, cervical, and axillary lymph node metastases, which occur in approximately 28 per cent of the cases. The next most frequent site of involvement is the liver, with the pleura, lung, bone, adrenal, kidney, brain and heart following in the order of their relative frequency.

In our series of cases the incidence of the various types of bronchogenic carcinoma in the proved cases is as follows: 14 were undifferentiated-cell type, 14 were squamous cell carcinoma and 4 were adenocarcinoma. Three of the adenocarcinomas occurred in women, and this corresponds to the usually reported high incidence of this tumor in that sex. One of our cases was unclassified histologically and in one other, in which the diagnosis was made by the presence of tumor cells in the pleural fluid, the cell type was not determined. We had one case of alveolar cell carcinoma. At the present time the histogenesis of this tumor is a matter of controversy. Some believe the tumor originates directly from the alveolar cells, but the majority of pathologists maintain that it arises from the basal layer of the bronchus in common with the other types of bronchogenic carcinoma.

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\*Acknowledgment. We wish to thank Dr. Joseph Kuzma, Director of Laboratories of the Milwaukee County Hospital, for assisting us in the pathologic classification.

### *Clinical Manifestation*

Early recognition of primary bronchogenic carcinoma is of vital importance if effective cure is to be obtained, therefore a review of the clinical features is important. Only four of the 47 cases were considered as operable at the time of admission. These patients were discharged to their private physicians, and on follow-up it was discovered that none had surgery. Two patients are alive at the time of this writing, both are inoperable.

There are many reasons for the excessively high incidence of inoperability in these cases. One was the delay by the patient in seeking medical advice. An average period of 6.4 months elapsed from the time of the first symptom. The second factor was the delay in establishing the diagnosis after the patient had consulted a physician. This period was 4.3 months, giving the total duration of symptoms 10.7 months before diagnosis was made. The total duration of life from the onset of symptoms to death was only 14.5 months. Bjork<sup>1</sup> reports almost the opposite findings in analysis of 112 cases, the patient's delay was 3.4 months, and the physician's delay was 5 months, giving a total of 8.4 months delay before the correct diagnosis was established. These observations emphasize the necessity of the development of cancer consciousness both in the physician and the public.

The clinical picture of primary bronchogenic carcinoma is mainly respiratory in character. The symptoms are cough, expectoration, chest pain, hemoptysis, dyspnea and wheeze. Cough is the most common symptom and it occurred as the presenting manifestation in 31 of our 47 cases. Usually a number of these symptoms occurred at the same time, and it was impossible for the patient to establish a priority. Other first symptoms that brought patients to the physician were chest pain in seven, hemoptysis, loss of weight and dyspnea in two each, and loss of strength in one. When any of the above symptoms occur, singly, or in a group, in an individual 40 years of age or over, bronchogenic carcinoma must always be considered.

Weight loss was a very prominent symptom, the average loss being 24 pounds. While most of our patients continued to lose weight, some have maintained or even gained weight when on a sanatorium regimen. One of our patients gained 22 pounds over a 3 month period and then suddenly developed lymphangitic spread of his carcinoma, simulating miliary tuberculosis, with a rapid downhill course to death. The gain in weight and the presence of acid-fast bacilli in the sputum culture confused the diagnosis. Subsequently, the micro-organisms were found to be nonpathogenic.

Unfortunately, the presenting symptoms may be due to metas-

tases to other organs. The bones, (ribs and spine are the most common) brain, or distant superficial lymph nodes (cervical, supraclavicular and axillary) are frequent sites. Most patients had some elevation of temperature, and the degree of elevation depended upon an associated pneumonitis. When bronchial obstruction was present, there usually was a septic type of fever varying from 100 to 103 degrees F.

Blood counts were of no diagnostic significance, and a moderate anemia was present in only 12 cases, varying from three to four million RBC per cu mm. Twelve other cases varied from 4 to 4.5 million RBC per cu mm. In the remaining 23 cases the count was over 4.5 million. The hemoglobin value corresponded with the red blood cell count. Leucocytosis was present in the majority of cases, 10 were in the normal range and the rest had over 10,000 white blood cells per cu mm. Twenty-three cases ranged from 16 to 26,000 WBC per cu mm. The differential WBC revealed a slight shift to the left in 14 cases. Henkin<sup>6</sup> reports a case in which the WBC rose to 85,000 and gradually dropped to 30,000 during a three month interval. Bone marrow puncture was not conclusive. However, bone metastasis was visible by roentgenogram five months after the height of the leukemoid reaction. He also states others<sup>6a, b</sup> have reported similar leukemoid reactions in bronchogenic carcinoma.

The blood sedimentation rate was rapid in 12 of 14 cases in which it was determined. Two cases had a normal rate. Only two patients were tuberculin tested before admission, and both of these were positive. Of our 47 cases, 27 were tuberculin positive, 9 were negative and 11 were not tested after admission. Of the nine negative cases, five were negative to PPD<sub>3</sub>, three to PPD<sub>1</sub> and one to 1-10 Old Tuberculin. One of the patients who did not react to PPD<sub>2</sub> was moribund, the other nonreactors were in good clinical condition. Obviously these negative reactors should never have been admitted to the sanatorium. This emphasizes the need and importance of tuberculin testing adults before making a diagnosis of pulmonary tuberculosis.

Pleural effusion was noted in 13 patients while under our observation and one had a bilateral effusion. Hemorrhagic pleural fluid is by no means always present. Ten of the effusions were aspirated, and clear or slightly cloudy fluid was obtained in eight, grossly hemorrhagic fluid in two. The differential cell count of the pleural fluid is not significant. In six cases the cell count revealed a lymphocyte count of 90, 83, 70, 35, 18, and 13 per cent. The first three counts would suggest a tuberculous effusion. One count revealed 60 per cent eosinophils, a very unusual finding. Tumor cells were present in six of the 10 cases examined. The

presence of tumor cells signifies metastasis to the pleura, and it is considered a contraindication to surgery. Not all pleural fluids contain tumor cells, small collections of fluid may be present along with atelectasis. This in itself would not constitute a contraindication to surgery. In our series, nine supraclavicular and cervical lymph nodes were positive on biopsy, and one inguinal lymph node was negative.

Seven of the 47 patients were sent to Muirdale Sanatorium because of positive sputum. Four of these cases had postmortem examination, and in only two could tuberculosis be demonstrated grossly and microscopically. In the three other instances we could not duplicate the positive results although numerous sputums and gastric aspirations were negative for acid fast bacilli. In view of our negative results we ignored the outside findings and considered them as inaccurate.

### *Diagnosis*

Physical examination has marked limitations. Frequently no abnormal findings are noted. The latter depend upon the volume and location of the tumor tissue and upon the degree of bronchial obstruction with an associated atelectasis, bronchiectasis and pneumonitis. The presence of localized rhonchi, which may be associated with a respiratory thrill, may be the only indication of a partial bronchial occlusion. Clubbing of the fingers was noted in 10 of the 47 cases. This has no significance in itself, and merely indicated pulmonary diseases. However, the widely held belief that clubbing rarely or never occurs in bronchogenic carcinoma is erroneous.

A roentgenogram of the chest is paramount, and the examination of any patient is incomplete without one. The radiological manifestations will, of course, depend upon the stage of the disease. Early, there may be no abnormality, but, unfortunately, these cases are rarely seen. It may be necessary to employ various positions and techniques, including tomography,<sup>8,9</sup> to visualize the lesion properly. In one of our cases, the latter procedure revealed a rib metastasis, otherwise obscured by a dense tumor mass. Bronchography is occasionally useful, and is of particular value in early, upper lobe and peripheral lesions. A perihilar mass is the most characteristic manifestation. There may be evidence of atelectasis, pneumonitis or emphysema. A single peripheral nodule may occur but this is relatively infrequent. Atelectasis was present in 25 of our 47 cases, obstructive emphysema was observed only twice. In a rapidly growing tumor central necrosis may occur and a cavity may be found. This was present in three of our cases.



Bronchogenic carcinoma may simulate any pulmonary lesion and should always be considered as a diagnostic possibility

Bronchoscopy is also paramount. It not only affords an opportunity for a biopsy but also gives the surgeon information as to the state of the carina and trachea. If they are invaded, the primary tumor is not resectable. A positive bronchoscopic biopsy will be obtained in about 50 per cent of the cases. Meade<sup>10</sup> in a report to the American Trudeau Society, states that there was about a 45 per cent positive bronchoscopic biopsy out of a total of 518 cases collected from three different authors. Thirty-four of our 47 cases had a total of 43 bronchoscopies. Twenty-two had biopsies and of these 16 were positive for carcinoma. In ten cases there was sufficient bronchoscopic evidence to indicate bronchogenic carcinoma. Eight patients had negative bronchoscopic examinations, however, negative bronchoscopic findings do not necessarily mean the absence of malignancy. Upper lobe lesions are difficult to visualize and peripheral lesions are practically never seen.

Tremendous advance has been made in the past few years in the cytological examination of bronchial secretions and sputum for tumor cells. The reports are very gratifying and various examinees<sup>11 13</sup> report positive findings varying from 80 to 90 per cent. According to Clerf,<sup>12</sup> cytological examination has conclusively demonstrated that carcinoma can be diagnosed in an additional 20 to 25 per cent of the cases whose lesions are beyond bronchoscopic vision.

An exploratory thoracotomy is a diagnostic procedure and should be resorted to in the presence of radiological evidence of a persistent or progressive pulmonary lesion in which all other diagnostic procedures have been negative, and in which all other causes of the lesion have been ruled out. There should not be too much delay in this decision, because metastasis may occur at any time.

We are in agreement with Jones<sup>14</sup> and others<sup>15 16 2</sup> that needle biopsy as a diagnostic procedure is a dangerous procedure and should not be used.

The treatment for bronchogenic carcinoma is surgical. Total pneumonectomy with resection of the bronchial and mediastinal lymph nodes is the usual procedure. Contraindications to surgery are paralysis of the diaphragm or vocal cords, metastasis, pleural effusion with the presence of tumor cells, involvement of the carina or trachea and very poor general condition of the patient. Some surgeons<sup>2</sup> do not necessarily consider paralysis of the diaphragm or vocal cords as a contraindication to surgery. Age is no contraindication. The incidence of resectability at the time

of diagnosis varies, according to Ochsner and his associates<sup>2</sup> it is one out of three patients, and according to Lambert,<sup>17</sup> one out of five. Only 4 of our 47 cases were considered operable, however, as previously stated, none of these had surgery. The operative mortality as reported in the literature varies from 20 to less than 4 per cent.<sup>14</sup> In a series of 412 cases Ochsner and his associates report a five year survival rate of 8 per cent.

It is generally recognized that roentgenray therapy is only palliative, and is used for the relief of intractable pain or secondary pulmonary infection.

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\*Dr J. D. Steele of the Surgical Department of Murrdale Sanatorium performed all the bronchoscopies.

### SUMMARY

In an eleven year period at Murrdale Sanatorium, 47 cases of primary bronchogenic carcinoma were observed. These patients were sent in as cases of pulmonary tuberculosis. Thirty-five of the 47 cases were proved by postmortem examination, biopsy and one by the presence of tumor cells in the pleural fluid. Twelve cases were diagnosed on the basis of clinical, roentgenologic and bronchoscopic findings.

Two cases had both pulmonary tuberculosis and primary bronchogenic carcinoma.

The average age of our patients was 55.4 years. Our youngest patient was 40 years old and the oldest was 73 years of age. The ratio of male to female was 3 to 1.

Of the proved cases, 14 were squamous cell type, 14 undifferentiated-cell carcinoma, 3 adenocarcinoma and one alveolar cell carcinoma. Two cases could not be classified histologically.

The importance of early recognition of primary bronchogenic carcinoma is emphasized by the fact that only four of the 47 patients were considered operable at the time of diagnosis. The interval from diagnosis to death was only 3.8 months, while a period of 10.7 months elapsed from the onset of symptoms to diagnosis. The patient's delay in seeking medical advice was 6.4 months and the physician's delay in establishing the diagnosis was 4.3 months.

The clinical picture of primary bronchogenic carcinoma is mainly respiratory in character, the prominent symptoms are cough, chest pain, hemoptysis, dyspnea. Weight loss was a constant finding.

Fever and leucocytosis depend upon the presence of secondary pneumonitis. No significant anemia was noted in any of our cases.

The importance of tuberculin testing adults is re-emphasized. Nine of our patients had negative tuberculin test and should never have been considered as tuberculous.

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The differential cell count of the pleural fluid revealed a marked lymphocytosis in three cases. Lymphocytosis is considered typical of tuberculous pleurisy with effusion and in these cases could mislead one to an erroneous conclusion.

Clubbing of the fingers is not an unusual finding in bronchogenic carcinoma.

The importance of roentgenograms, bronchoscopy, cytological examination of sputum and bronchial secretions and thoracotomy as diagnostic procedures are discussed.

### RESUMEN

En un período de once años se observaron 47 casos de carcinoma broncogénico primario en el Sanatorio de Murrumbidgee. Estos pacientes fueron enviados al sanatorio como casos de tuberculosis pulmonar. Se comprobó a 35 de los 47 casos mediante el examen autopsico o la biopsia y a uno por la presencia de células malignas en el derrame pleural. Se diagnosticó a 12 casos a base de los hallazgos clínicos, roentgenológicos y broncoscópicos.

Dos casos tenían tuberculosis pulmonar y también carcinoma broncogénico primario.

La edad media de nuestros pacientes fue de 55.4 años. Nuestro paciente más joven tenía 40 años y el más viejo 73 años de edad. La proporción de hombres a mujeres fue de 3 a 1.

De los casos comprobados, 14 fueron de tipo de célula escamosa, 14 carcinomas de célula no diferenciada, 3 adenocarcinomas y uno carcinoma de célula alveolar. No se pudo clasificar histológicamente a dos casos.

Lo importante del reconocimiento temprano del carcinoma broncogénico primario lo recalca el hecho de que a sólo cuatro de los 47 pacientes se les consideró operables cuando se les hizo el diagnóstico. El intervalo del diagnóstico a la muerte fue sólo 3.8 meses, mientras que un período de 10.7 meses transcurrió desde el comienzo de los síntomas hasta que se hizo el diagnóstico. La demora del paciente en consultar al médico fue 6.4 meses y la demora del médico en establecer el diagnóstico fue 4.3 meses.

El cuadro clínico del carcinoma broncogénico primario es principalmente de carácter respiratorio, los síntomas prominentes son tos, dolor en el pecho, hemoptisis y disnea. La pérdida de peso fue un hallazgo constante.

La fiebre y la leucocitosis dependen de la presencia de neumonitis secundaria. No se notó anemia significativa en ninguno de nuestros casos.

Se recalca de nuevo la importancia de comprobar con tuberculina a los adultos. Nueve de nuestros pacientes eran negativos.

a la tuberculina y nunca se les debería haber considerado ser tuberculosos

La enumeración diferencial de las células del derrame pleural reveló decidida linfocitosis en tres casos. Se considera que la linfocitosis es típica de la pleuresia tuberculosa con derrame y en estos casos habría podido conducir a conclusiones erróneas.

El ensanchamiento de la punta de los dedos no es un hallazgo raro en el carcinoma broncogénico.

Se discute la importancia de los roentgenogramas, la broncoscopia, los exámenes citológicos del esputo y de las secreciones bronquiales y la toracotomía, como procedimientos diagnósticos.

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# Pathogenesis of Pulmonary Atelectasis

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Before discussing the pathogenesis of atelectasis, three illustrative cases are described, each having a different aetiology. It is proposed to show later that even though the precipitating factor in each of the cases is different, the ultimate mechanism by which atelectasis is produced is essentially the same.

*Case 1* Male, 26 years, was admitted to hospital for fever and cough of 10 days duration. The fever was continuous and ranged between 100 and 102° F. Respiration was not hurried. A diagnosis of bronchiolitis was made. A week later the condition of the patient became worse. The range of temperature was higher. His breathing also was a bit more hurried. On examination a triangular area of dullness in the left base behind, with bronchial breath sounds and a few moist sounds were found. X-ray picture (Fig 1) showed a triangular opacity overlapping the left border of the heart. In the lateral view the opacity was found to be situated posteriorly. A diagnosis of left lower lobe atelectasis was made. As the total leucocyte count was 14,000, he was put on sulphapyridine, the temperature decreased by lysis. His signs and symptoms disappeared only eight weeks after admission. X-ray picture taken at that time showed that the opacity had disappeared (Fig 2).

*Case 2* Male, 33 years, gave a history of a fall during which the left side of his chest struck against a projecting stone. Pain was so severe that he had difficulty in breathing for some time. There was no external injury. He spat out a little blood-tinged mucous after the injury. The pain lasted for a week. Subsequently he developed cough with expectoration. He had no fever. A few moist sounds were heard in the left base, but no other physical signs could be elicited. An x-ray picture (Fig 3), however, showed a narrow well defined triangular opacity overlapping the cardiac shadow in the left side. The diagnosis of left lower lobe atelectasis was confirmed by a lateral x-ray picture.

*Case 3* Male, 24 years, had a fish bone admitted to the air passage while swallowing. He experienced difficulty in breathing and aching pain in the right side of the chest. Fever and cough started the next day. A few days later he began to expectorate purulent sputum. Examination revealed impaired resonance and bronchial breath sounds over the right base. X-ray picture showed a triangular opacity in the right cardiophrenic angle continuous with and obliterating the right border of the heart. Lateral view confirmed the diagnosis of right lower lobe atelectasis. Conservative treatment and postural drainage cleared up the condition in 6 weeks so the x-ray picture showed no opacity.

Intrapulmonary inflammation in the first, external thoracic injury in the second and frank bronchial obstruction by a foreign body in the third case brought about the same condition, namely lower lobe atelectasis. Inflammatory exudate in the first case in all probability produced multiple bronchiolar obstruction while haemorrhagic mucous secretion was the obstructing agent in the second case. The object of this paper is to show that bronchial or bronchiolar obstruction is the main contributing factor in the mechanism of collapse and that it brings about the condition in two entirely different ways.

*Current Theories* The pathogenesis of pulmonary atelectasis has been a subject of discussion for over a century. Even the earliest observers like Reynaud (1835) and Hasse (1846) recognized the importance of bronchial obstruction in the aetiology of atelectasis. Gairdner (1850) regarded the blockage of bronchial tubes by retained secretion as the cause of collapse. Pasteur (1908) having seen massive collapse of the lung occurring during diphtheritic paralysis, postulated the theory of diaphragmatic paralysis to explain the occurrence of postoperative atelectasis. The experimental work of Briscoe (1919) appeared to confirm this theory. He pointed out that, in the supine position, the inspiratory movements of the diaphragm are ordinarily carried out by the crura

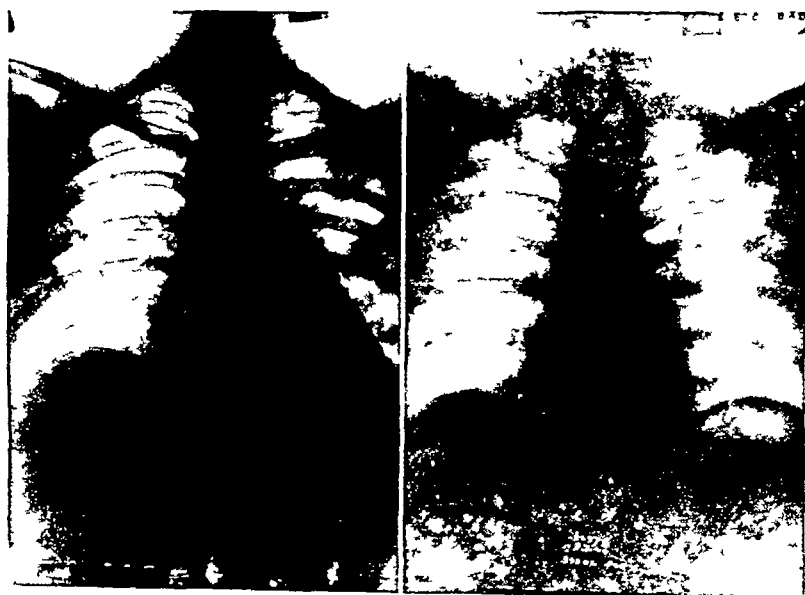


FIGURE 1

FIGURE 2

Figure 1 Case 1 Note the triangular opacity in the left cardiophrenic angle. Left dome of diaphragm raised—Figure 2 Case 1 Note the disappearance of the opacity. Lower lobe has expanded.

and not by the costal attachment. Continued supine position might produce a certain degree of collapse which will be aggravated by irritation of the diaphragmatic pleura near the crura after abdominal operations. While Pasteur and Briscoe emphasized the importance of paralysis of respiratory muscles, Elliott and Dingley (1914) laid great stress on the importance of bronchial obstruction as the chief contributing factor.

A fresh stimulus to the study of massive collapse was given by Rose Bradford (1918) who observed a series of cases of collapse following nonpenetrating injuries to the chest during the Great War of 1914 to 1918. The chief explanation suggested by him was a reflex paralysis of the respiratory muscles. Those who have observed basal pulmonary collapse associated with infection of nasal sinus, also postulate reflex nervous stimulus as the causative mechanism. Coryllos and Birnbaum (1928) produced occlusion of the main bronchus by means of an air inflated balloon which caused pulmonary collapse in 6 hours. Jacobaeus (1930) noted massive collapse in the human subject within 10 minutes after introduction of lipiodol.

The most notable contribution to the knowledge of the subject has been made by Chevalier Jackson who emphasises the supreme



FIGURE 3



FIGURE 4

*Figure 3, Case 2. Note the well marked triangular opacity inside the cardiac shadow in the left side—Figure 4, Case 3. Note the triangular opacity in the right cardiophrenic angle. Outline intensified by touching.*

importance of bronchial obstruction in producing atelectasis Removal of a foreign body in the bronchus is followed by rapid disappearance of collapse Jackson has shown that collapse in diphtheria is not due to paralysis of diaphragm but to obstruction of the bronchus by membrane and agglutinated mucous When the obstruction was removed by the bronchoscope the symptoms and signs speedily cleared up According to him cough reflex is the watch dog of the lungs and when that reflex fails the lumen becomes completely obstructed It is interesting to note that as early as 1853 Gairdner gave the three chief causes of pulmonary collapse in infancy as, mucous in the bronchi, weakness of the respiratory muscles, and inability to cough

Hilding (1944) dissatisfied with the explanation of bronchial obstruction, has put forward a fascinating theory based on some convincing experiments by which he has shown that loose mucous plugs can be moved up from the distal to the proximal ends of the bronchi and bronchioles through ciliary action These mucous plugs act like pistons and as they move up one after the other columns of air are removed from the affected lobe until the latter is collapsed completely The theory is ingenious It cannot how-

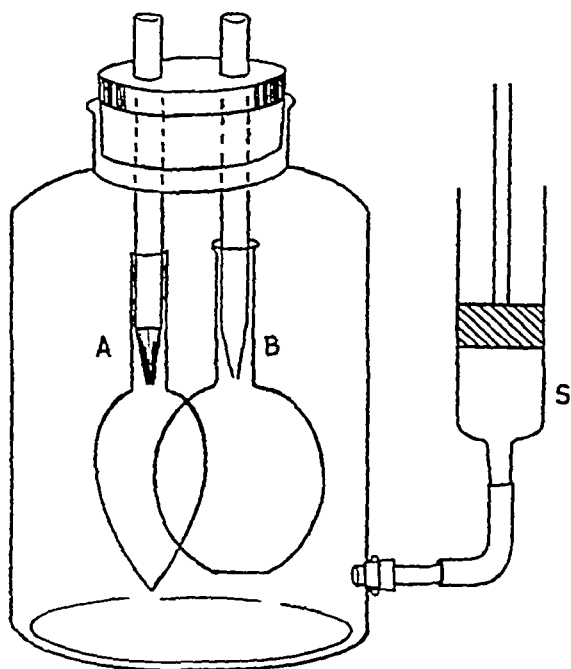


FIGURE 5 *Pulmonary Atelectasis Laboratory Experiment* Figure represents the state of the bladders at the termination of the experiment Note A' in which the bladder is collapsed owing to presence of secretion in the glass tube In B the bladder is distended as there is no obstruction S represents the syringe



ever explain the mechanism of collapse in all cases. His statement that air cannot be absorbed by the blood in the lung capillaries is disproved by the experimental production of collapse by complete obstruction to a bronchus. In such a case, air could have disappeared from the alveoli only by its being absorbed into the blood stream.

The mechanism of collapse in case of complete obstruction of the bronchi, either intrabronchial as by foreign body or extrabronchial as by tumour, is easily understood. Air in the obstructed lobe has necessarily to get absorbed into the blood stream. Doubts and difficulties however arise when one tries to work out the process by which portions of lung become airless in nonpenetrating chest injuries, in pulmonary inflammations and after abdominal operations. When the theories so far advanced to explain the pathogenesis of massive atelectasis are analyzed, they are found to fall into two broad groups, namely bronchial obstruction and respiratory paralysis. Paralysis chiefly of the diaphragm is brought about according to different theories in different ways. It might be a reflex mechanism, or an allergic response, or a true nerve paralysis as in diphtheria. The theory of respiratory paralysis as the sole cause of atelectasis cannot be substantiated. Respiratory paralysis no doubt will abolish any movement of air in the alveoli. Air in the alveoli in the natural course of events will be absorbed into the blood stream. It will however be replaced by outside air so long as there is no obstruction in the air passages. Hence the lung cannot collapse simply as a result of paralysis of respiratory muscles. Moreover, massive collapse of the lung is not seen to occur after phrenic evulsion. Paralysis of the diaphragm produces only a relaxation of the lung and does not cause all the air to disappear. Besides, neither in postoperative conditions, nor after external chest injuries, do the respiratory muscles get so completely paralyzed as to cease functioning. Only reflex inhibition of respiratory movements and not total abolition, occurs in these conditions. In fact, according to the theory propounded below, a certain amount of respiratory excursion is required to produce pulmonary atelectasis.

The protagonists of the bronchial obstruction theory believe that complete blocking of the bronchi or bronchioles by thick mucous secretion and subsequent absorption of air from the alveoli into the blood stream are the processes concerned in the production of atelectasis. It has been seen no doubt that this is the mechanism in case of foreign body obstruction of the bronchi. I am, however, not convinced that mere mucous secretion, however viscid, it might be, can produce complete bronchial or bronchiolar obstruction. Hilding has shown that through the muco-ciliary mechanism,

secretion can be moved up the bronchioles Moreover, a fairly forcible current of air sufficient to dislodge mucous secretion passes to and fro during the process of respiration through the narrow bronchial or bronchiolar passage Another point against the theory of complete obstruction is the length of time required to produce atelectasis In Coryllos' experiment of bronchial occlusion it took nearly six hours to produce atelectasis

Jacobaeus, on the other hand, observed atelectasis occurring within ten minutes after intrabronchial installation of lipidol The onset of posttraumatic and postoperative atelectasis is also equally sudden and rapid It is obvious therefore that the process of absorption of air into the interalveolar blood stream cannot explain such rapid disappearance of air from the lung as it occurs in the above mentioned conditions What then is the mechanism by which massive atelectasis is produced?

The theory which I wish to put forward as a rational and adequate explanation is substantiated by experiments performed on the human body immediately after death and on animals under anaesthesia, as well as by laboratory experiments I agree with Jacobaeus and Jackson that bronchial or bronchiolar obstruction is a necessary condition to be satisfied before atelectasis occurs Secretions in the bronchial tubes both in post-traumatic as well as postoperative conditions are the obstructing agents Accumulation of secretion is no doubt caused by diminished respiratory excursion If the process of rapid disappearance of air from the lung is to be understood the essential prerequisite of some respiratory movements should be granted I contend that the mucous secretions in the bronchioles instead of producing complete obstruction act like ball-valves allowing air to get out from the lung during expiration but preventing air to get in during inspiration The ball-valve-like action can readily be conceived because the bronchi are not of the same calibre throughout their length The distal portions are narrower than the proximal portions Hence it is easy to imagine how a plug of mucous can effectively block a bronchus or bronchiole as it is moved distally by the inspiratory air current and how on the other hand it will allow air to pass through when it is moved towards the broader proximal end If for instance the lower lobe bronchus is blocked by a mucous plug some amount of air will be expelled during expiration as a result of the plug being moved to the broader proximal portion of the bronchus and thereby rendering it patent During inspiration, however, air is not allowed to enter, and the lower lobe to that extent is partially collapsed If a hundred cc of air gets into one lung during each inspiration, all the hundred enters the upper lobe if the lower lobe bronchus is blocked During the next expira-

tion as the intra-alveolar air pressure throughout the chest cavity is higher than the atmospheric pressure, air gets expelled from all the lobes irrespective of whether any one of them is partially collapsed. Hence more air passes out from the lower lobe during expiration than is replaced during inspiration. With every act of respiration the lower lobe becomes more and more collapsed and the process continues until it is completely airless. The mechanism is facilitated by the inherent tendency of the lung to shrink owing to its elasticity. It is quite conceivable how by this process atelectasis can be produced in a few minutes provided there is ball-valve-like obstruction to the bronchus and the integrity of respiratory excursion is maintained. Without respiratory movements rapid disappearance of air from a partially obstructed lobe cannot be produced. If a valvular opening in lung rupture can produce a tension pneumothorax, I see no reason why a ball-valve obstruction to the bronchus cannot produce rapid atelectasis. In fact it is not possible to conceive of any other way by which air can completely disappear from a lobe within the short period of ten minutes or even less. Absorption into the blood stream is out of the question as it has been shown by Ceryllos that it takes nearly six hours for atelectasis to be produced by complete obstruction, during which time air is absorbed into the blood.

Even the presence of liquid secretion in the bronchiole under favorable circumstances will contribute to establish a one-way traffic for the air which might bubble out through the fluid during expiration but is unable to get into the affected alveoli during inspiration. This is facilitated by the decreasing calibre of the distal portions of the bronchi and bronchioles. Each of these is in the shape of a narrow, more or less conical tube. If it contains fluid secretion the air from the alveoli attached to its narrow end can bubble through, but air coming from outside through the proximal end will not be allowed to pass as the fluid will be driven to the narrow distal end where it will form an effective block for the air. In the case of multiple lobular atelectasis after drowning, described previously by the writer (1941), sea-water acted as the obstructing medium and evidently operated by the above described mechanism. It is obvious that not only should there be an obstructing agent in the respiratory passages but the respiratory movements should be maintained as well.

The following experiments were performed to substantiate the theory described above.

- 1) The first experiment was on a human body immediately after death. Materials required were previously prepared as the time of death was anticipated. The trachea was opened and a rubber tube introduced into the right bronchus. Twenty cc of an

oil emulsion of the consistency of lipiodol was introduced through the tube. Artificial respiration by the writer's method (1945) was given for five minutes. The trachea was then plugged air-tight with a cork and the chest opened in the usual manner. The right lower lobe was found to be distinctly, though partially collapsed, while the left lung and right upper lobes remained distended owing to the trachea being plugged. Evidently the emulsion had gone into the right lower lobe bronchus and produced the necessary block. With the help of artificial respiration and blockage of the bronchus collapse of the lower lobe was obtained.

Keeping the thoracic structures in situ the left bronchus was opened and two rubber tubes were introduced into the upper and lower lobe bronchi respectively and pushed so as to make them fixed inside. The free ends of the tubes were connected to the limbs of a Y-shaped nozzle whose opposite end was connected to the exit end of a Higginson's syringe. Air was pumped in, to make the lobes partially distended. The tube to the lower lobe bronchus was disconnected from the nozzle and after a few cc of soft soap emulsion was introduced, it was reconnected. Air was pumped in with the aid of the syringe. It was found that while the upper lobe was getting distended the lower lobe remained as it was. The Higginson's syringe was disconnected and uniform pressure was applied to both of the lobes, which collapsed. When more air was pumped in the upper lobe alone expanded while the lower lobe remained collapsed occupying a posterior position in the chest cavity.

2) A simple laboratory experiment was designed to show the mechanical nature of the process involved in the production of atelectasis. A large wide-mouthed jar with a narrow side-opening near the bottom was chosen. It was fitted with a cork with two perforations through which two glass tubes were introduced. Each tube tapered to a capillary end. A small football bladder was fitted to each of the tubes so that the bladders remained suspended inside the jar. The lower opening in the jar was closed with a cork to which a glass tube was fitted. The outer end of the glass tube was connected to rubber tubing to whose free end was fitted the lateral nozzle of a Potain's aspirator. The air from the jar was aspirated to such an extent as to produce moderate distension of the bladders. The aspirator was then removed and the nozzle of an ear syringe was fitted to the rubber tube. By working the piston to and fro a bellows action could be produced so as to increase or decrease the pressure of air inside the jar to an equal measure each time. The result was, the bladders contracted or expanded as the pressure of the air inside the jar increased or decreased. The jar represented the chest and the

bladders represented two lobes of a lung The glass tubes fitted to the bladders represented the bronchi

Into one of the glass tubes was introduced a small mucous plug from the sputum of a patient The syringe was worked slowly at the rate of 18 per minute It was found that the bladder connected to the glass tube into which the mucous plug was introduced contracted each time when air was pumped into the jar, but failed to expand when the process was reversed The result was the bladder shrank in size while the other bladder expanded more and more

The experiment was repeated with a viscid fluid inside one of the glass tubes It was not successful as it was found that the fluid was gradually getting aspirated into the bladder through the capillary opening The tubes being vertical, the action of gravity helped in driving the fluid through In order to overcome this difficulty the jar was kept slanting about 5 degrees from the horizontal This would have more or less corresponded to the recumbent position of a patient in bed As the action of gravity was almost overcome in this manner, the experiment succeeded The air from the bladder bubbled out through the fluid during the process of contraction The fluid however effectively blocked the passage of air back into the bladder The same results as in the experiment with the mucous plug were obtained

It has been conclusively proved by the above experiments that obstruction to the bronchi either with semisolid or fluid material, recumbent posture and shallow respiration are the necessary and sufficient conditions to produce atelectasis of the lung

3) A dog was anaesthetized Chloroform was used so as to produce shallow respiration The trachea was opened at the lowest possible level and a rubber catheter was introduced into the right bronchus, ten cc of viscid sputum were introduced through the catheter The dog was kept under for another ten minutes, during which period shallow respiration was maintained The dog was killed by deepening the anaesthesia The trachea was firmly plugged with a cork so as to allow no air to escape from the lungs consequent on their shrinking during opening of the chest cavity On post-mortem it was found that the lower lobe of the right lung was almost completely collapsed

All the experiments described above conclusively substantiate the theory propounded in this paper The pathogenesis of atelectasis can be briefly summarized as follows Taking postoperative atelectasis as an example, the process starts with accumulation of secretion in the bronchi and/or bronchioles This is facilitated by diminished respiratory movements and temporary dysfunction of the muco-ciliary mechanism Owing to progressive distal nar-

rowing of the bronchioles, the secretion effectively blocks the air getting into the alveoli during inspiration, but allows it to escape outside during expiration. This process therefore depends on the integrity of the respiratory movements; however shallow they might be. After repeated acts of respiration the affected lobe becomes collapsed.

Apart from post-anaesthetic conditions, restriction of respiratory movements can be produced through pain, either pleuritic or post-traumatic. Excessive secretion necessary for blockage can be produced either by bronchiolar inflammation as in the first case or posttraumatic haemorrhage as in the second. The mode of production of atelectasis in the third case was similar to that in Coryllos' experiment, namely complete bronchial obstruction and subsequent absorption of air into the blood stream. The more frequent occurrence of lower lobe atelectasis particularly in post-operative conditions, is due to several factors. The whole of the posterior surface of the lower lobe is in contact with the back of the chest and practically the whole of the diaphragmatic surface of the lung is formed by the lower lobe. When the back is fixed in the recumbent position, if the diaphragmatic movement also is restricted either through post-anaesthetic shallow breathing or through tight abdominal bandaging, the respiratory excursions of the lower lobe will be rendered relatively smaller than that of the upper lobe. Hence stasis of secretion occurs more easily in the lower lobe bronchioles. Moreover the lie, direction and inclination of the lower lobe bronchus and its branches are more favorable to the production of ball-valve action of the secretion inside them. Lower lobe atelectasis is therefore less likely to happen if the patient, after operation, is propped up or turned to one side or the other. Perhaps by keeping the patient in the Trendelenburg position until normal breathing is established, pulmonary atelectasis might be prevented, as it will prevent accumulation of secretion in the lower reaches of the bronchioles.

### SUMMARY

- 1) Three cases of lower lobe atelectasis are described.
- 2) A short review of the available literature on the pathogenesis is given.
- 3) The writer is of the opinion that establishment of one-way traffic for the air in the bronchioles by the presence of secretion inside is the cause of pulmonary atelectasis. Respiratory movements are none the less necessary.
- 4) Experiments are described to substantiate the theory.
- 5) Reasons for relative frequency of lower lobe atelectasis are cited.

## RESUMEN

- 1) Se describen tres casos de atelectasia del lóbulo inferior
- 2) Se presenta una corta revista de la literatura obtenible sobre la patogenia de este estado
- 3) El autor opina que el movimiento del aire dentro de los bronquios, debido a la presencia de secreciones, es la causa de la atelectasia pulmonar Sin embargo, los movimientos respiratorios también son necesarios
- 4) Se describen experimentos que verifican esta teoría
- 5) Se citan varias razones para explicar la relativa frecuencia de la atelectasia del lóbulo inferior

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# Lipoid Pneumonia in Neuropsychiatric and Debilitated Patients

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Lipoid pneumonia is a relatively recent clinical entity which has attracted much attention in medical literature in the past two decades and during the last year the dangers associated with continued and excessive use of mineral oil have been stressed<sup>3</sup> Formerly believed to be a disease among children following the use of oily nose drops, the condition is not as uncommon in adults as was previously thought<sup>4</sup>

The four cases presented in this paper were collected from seventy-three consecutive autopsies performed at this hospital It is not surprising that lipoid pneumonia should occur with relative frequency in neuropsychiatric patients, particularly, where intellectual and emotional regression to the infantile level has taken place Feedings and medications can be administered to these patients often only when the greatest difficulty and the aspiration of oily medications is a constant hazard This is especially true in advanced bulbar palsies of various types where deglutition has been impaired and in those patients who are bedridden and confined to wheel-chairs The inactive patient is a constant feeding problem and often has sluggish, irregular bowel movements and is frequently in need of laxatives Mineral oil and cascara have been the favorite medications for this purpose over a period of years and were formerly considered innocuous, however, it has been amply pointed out by Sweeny<sup>10</sup> that mineral oil is often the offender in lipoid pneumonia In his compilation of one hundred and thirty-one adult cases he showed that the use of mineral oil as a laxative accounted for one half the series

## REPORT OF CASES

*Case 1* J T M, a 52 year old white male was admitted to the hospital in April 1939, in the advanced stage of postencephalitic Parkinson's disease, with marked impairment of locomotion, pill-rolling tremor, mask-like facies, and drooling at the mouth Hospitalization under close supervision was necessary to assist him in eating, bathing, and walking around the ward and grounds Medication consisted of atropine, hyoscine and various vitamin preparations Early in the course of hospitalization it

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was noted that the patient's bowel movements were irregular and mineral oil was given regularly once or twice a week

In January 1941, it was noted that the patient was becoming frequently subject to "colds" At this time he developed what was interpreted as a bronchopneumonia Mineral oil was continued in doses of one ounce twice a week In April 1942, a routine chest plate showed only slight peribronchial thickening, more marked in the right lung, which was interpreted as a low grade bronchitis

In December 1942, the patient developed his second bout of pneumonia The pneumonia lasted four days and the patient made an uneventful recovery Following this he developed a chronic cough

In January 1944, the patient developed his third attack of bronchopneumonia with an intermittent fever, sometimes reaching 105 degrees F The patient was critically ill but recovered after three weeks X-ray film at this time revealed moderate peribronchial infiltration confined mostly to the right middle and lower lobes It is of interest to note that in April 1946, two years and three months later, while the patient was supposedly completely well, a routine chest film revealed peribronchial infiltration at the right base and right middle lobe, similar to film taken during previous illness

The terminal illness began one year later with weakness, anorexia, high fever, and a rapid pulse Chest films taken at this time showed peribronchial infiltration involving primarily the lower lobes of both lungs, but more marked on the right where the upper lobe was also involved Rales developed in both bases and in spite of penicillin, fluids and oxygen therapy, the patient expired

Necropsy findings were essentially negative except for the lungs which were free in the pleural cavities and exhibited dark red color and boggy character characteristic of an advanced pneumonic process with consolidation Microscopic examination of the lung tissue revealed masses of polymorphonuclear leukocytes and debris filling the alveoli and bronchioles with a number of phagocytes filled with lipid droplets

*Case 2* J H, a 41 year old white male entered the hospital in April 1934 A diagnosis of Huntington's chorea was made and his course of hospitalization was that of a typical case with progressive mental enfeeblement and increase in neurological symptoms In October 1943, it was first noted that the patient had difficulty in swallowing food and medications Shortly thereafter his bowel movements became irregular and mineral oil and cascara were administered at regular intervals Mineral oil and cascara were given once a week every week for the last three years of his life

The patient continued to fail and one month before death developed a low grade fever and cough with moderate cyanosis and dyspnea A chest film at this time revealed a diffuse peribronchial thickening involving primarily the right middle and lower lobes with evidence of infiltration (Fig 1) In spite of specific and supportive therapy the patient expired

At necropsy the right lung appeared to be partially collapsed and lay in 800 cc of hemolyzed blood in the pleural cavity The entire middle lobe was dense and firm and on section it was yellowish and increased in consistency with no increase in fluid There was a fibrous exudate over the pleural surface with a few broken adhesive tags The left lung was bound down by firm adhesions laterally and the lower three fourths

showed decreased crepitus and was boggy and dark red, on section fluid was markedly increased with purulent areas. The pleural cavity was empty. Sections of the brain showed atrophy of the caudate nucleus and other findings characteristic of Huntington's chorea.

Microscopic study of lung sections showed pus cells in many alveoli often forming small abscesses. Macrophages filled with lipoid material or droplets, predominated in other areas. There was considerable fibrosis with thickening of the alveolar wall (Fig. 2).

**Case 3** S S, a 65 year old white male was admitted to the hospital with a right cerebral thrombosis. A few days after admission it was noted that the patient was constipated. Petrogalar and phenolphthalein were administered. For the next seven months the patient received these drugs in one ounce doses one to three times a week. The orders were then changed to mineral oil and cascara and this was administered once or twice a week for three months.

Five months later the patient developed his first attack of "pneumonia." At that time he complained of a pain in the left chest. He had a low grade fever, never exceeding 100.2 degrees F rectally. The chest findings were completely negative. A chest plate at that time was reported as normal. The patient was treated symptomatically with some improvement. He developed a hacking chronic cough productive of thick, white sputum. Six months later he again developed a pain in the left chest and a "cold." X-ray plate at this time showed "marked accentuation of the bronchovascular tree" and "increased density in the left

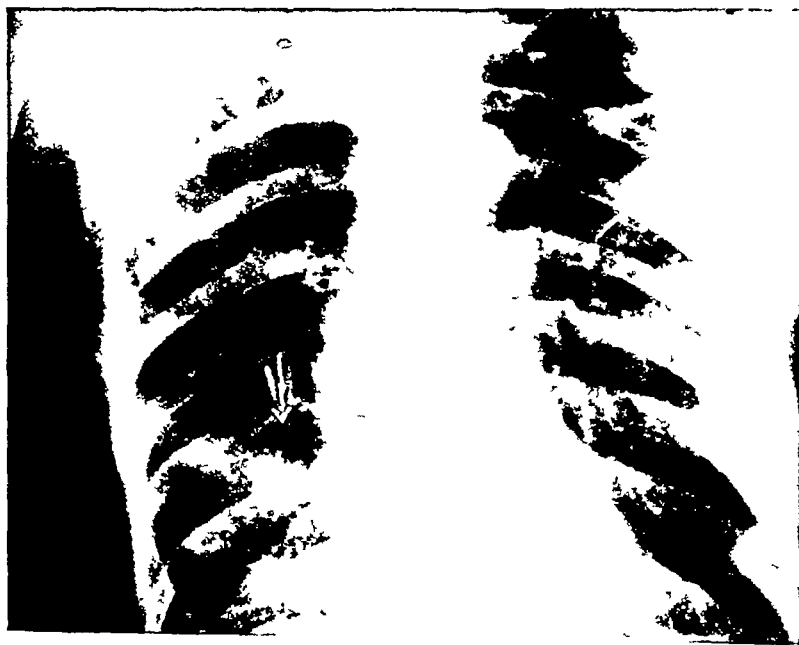


FIGURE 1 Chest plate of patient in Case II. Note peribronchial thickening in region of right cardiophrenic angle. There is a soft area of infiltration seen in the central portion of right lower lobe (arrow).

lower lobe suggesting pneumonitis" The patient recovered from this illness but his cough increased in frequency and severity

Eight months later the patient had another chest plate because of chronic cough and low grade fever This was read as "chronic bronchitis" and "slight infiltration in left lower lobe suggesting pneumonitis"

Four months before death, while the patient was considered asymptomatic, a routine chest plate was done during a tuberculosis survey This plate was identical with those taken during the episodes of "pneumonia" showing an increase in bronchovascular markings with a similar area of infiltration in left lower lobe

It is of interest to note that no oily substances were administered to the patient thirty months prior to his death In spite of this the patient's course was downhill He developed low grade fever, cyanosis, signs of respiratory embarrassment, and finally expired in spite of supportive therapy

The pulmonic pathological changes were of interest despite the apparent demise of the patient from a coronary accident The lungs were free in the pleural cavities which were empty Anthracosis was present, grade 2 The weight of the left lung was 480 grams and it contained many poorly outlined, rubbery nodules which varied between 1 cm and 4.5 cm in diameter They were grey against the more or less normal lung tissue which served as a pink background These nodules were scattered throughout all the lobes but were more numerous in the right lung which weighed 575 grams The right lower lobe was boggy and dark red in color with a marked increase in consistency

Microscopically the lung revealed a fibrous thickening of the alveolar

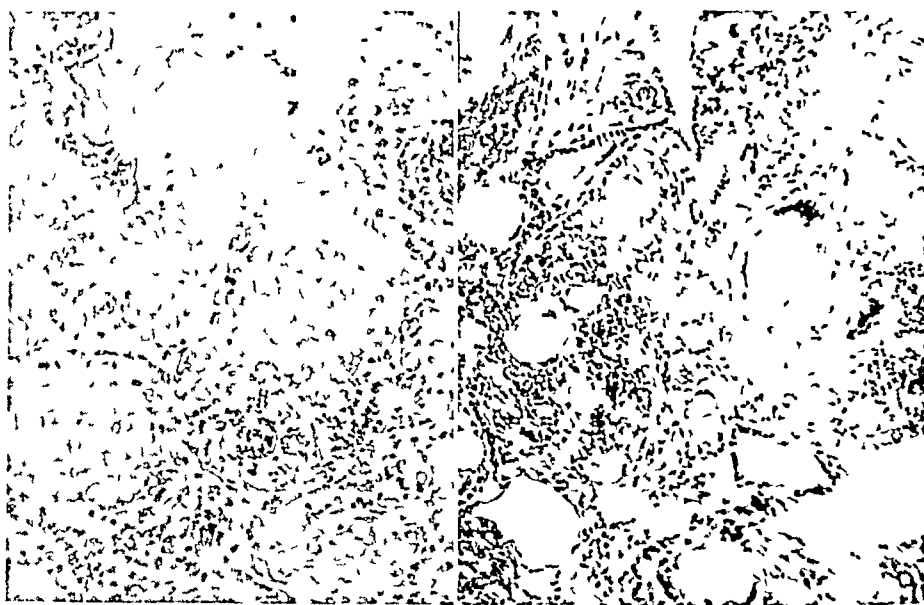


FIGURE 2

FIGURE 3

*Figure 2* Lung section from Case II The alveoli present a foamy appearance due to lipid-filled macrophages—*Figure 3* Section of lung from Case III The alveolar structure has been destroyed by proliferating fibrous tissue There are extensive lymphocytic aggregations There are numerous lipid spaces in the connective tissue and giant cells have formed about some of the larger droplets of oil

walls with obliteration of many alveoli due to the connective tissue proliferation. The connective tissue and alveoli contained numerous foreign body giant cells (Fig 3), many of these formed about circular clear spaces of varying dimensions which were assumed to be lipid or oil droplets and which were demonstrated as such in microscopic preparations stained with fat stains. Also present were many macrophages filled with lipid droplets.

*Case 4* C S, a 49 year old white male was admitted to this hospital in January 1944. The patient's grandmother, father, two sisters and two brothers had had Huntington's chorea. The patient developed choreiform movements twenty-two years prior to admission. These movements became progressively worse. He grew extremely irritable, depressed, and his reasoning and judgment became defective. He was admitted to this hospital for observation. Physical examination was essentially negative. Neurological examination revealed many choreiform, isolated and uncoordinated movements of all extremities. His speech was slurred and he had much difficulty in swallowing. The patient was given thiamin and nicotinic acid. Cod-liver oil was given twice a day, every day for forty-two days. Sixteen months after admission the patient developed a slight cough and began to run a low grade fever, never exceeding 100.6 degrees F rectally. This condition lasted about ten days and cleared spontaneously without treatment. The patient got along fairly well until April of 1947 when he developed a chronic, hacking cough which persisted until the time of death. One week before death the patient developed a low grade fever and his cough increased. Coarse rales were heard at both bases. His color was ashen gray and the lips cyanotic. Supportive treatment was of no avail and the patient expired. No oily medications had been administered to this patient for thirty-one months previous to death. X-ray plates taken at intervals during hospitalization were unsatisfactory because of inability of patient to remain quiet enough for the exposure.

At necropsy the most pertinent findings were those of a bronchopneumonia. Of added interest was atrophy of the caudate nucleus with consequent internal hydrocephalus, so characteristic of Huntington's chorea. The lungs were small, the right weighing 330 grams. The upper lobe was aerated and pink, the lower lobes were darker and crepitus was absent in these two lobes. Fluid was slightly increased on cross section and froth decreased. The left lung weighed 605 grams, was reddish-brown on the pleural surface and on section it was firm and noncrepitant and was apparently the result of a well established pneumonic process. Microscopic examination of the lungs revealed many lipid-filled macrophages in the alveoli with some monocytes and polymorphonuclear leukocytes.

### *Incidence*

The reports of the incidence of lipid pneumonia have varied and in many instances have included the type that occurs commonly in infants. This would tend to make the cases more numerous, however, in the last two decades, following the work of Laughlen<sup>6</sup> in 1923, the use of oily nose drops in children was widely and generally condemned so that recent studies should show but very few cases in this age group. Pinkerton<sup>9</sup> in 1927,

noted six cases in 290 consecutive necropsies, an incidence of 2 per cent Ikeda<sup>5</sup> in 1935, found an incidence of 7 per cent in children, and encountered five adult cases in an unrecorded series of necropsies, but no single instance in a series of thousands performed before 1932 Freiman et al<sup>4</sup> in 1940, found 12 per cent in a series of 3500 necropsies in adults and Cannon<sup>2</sup> recorded a percentage almost similar in 2000 adults The four cases presented represent approximately 5.4 per cent in a consecutive series of necropsies

### *Diagnosis and Clinical Course*

It has been estimated that approximately one fourth of the cases are considered asymptomatic as far as the lipoid pneumonia is concerned, but often a careful review of the history following necropsy will reveal that what appeared to be a spontaneous bout of terminal pneumonia was actually the last of a series of pneumonic attacks over a long period of time which were superimposed on the fertile soil of a long-standing lipoid affair A history of repeated respiratory and pulmonic infections, with a chronic cough between bouts, particularly in those individuals taking large amounts of mineral oil, cod-liver oil, or oil-agar preparations, should always suggest a lipoid pneumonic process as a predisposing factor and serial x-ray films taken over a period of time should lend further support to and increase the incidence of antemortem diagnosis Patients with dysphagia are particularly prone to this disorder as well as the debilitated and bedridden patient who is constipated and who often is a feeding problem as well The presence of oil in the sputum after the intake of oil, milk, cream or other fats have been restricted for some time is often of diagnostic importance, either by centrifugalization and the use of fat stains, or by observing the oil drops on a bit of cigarette or tissue paper immersed in the specimen Aspiration biopsy of the lung has also been suggested by Nathanson and his associates<sup>8</sup> but one must consider that one might readily strike relatively normal areas due to the patchy distribution

### *Roentgenological Findings*

Moel and Taylor<sup>7</sup> aptly called attention to the main roentgen findings in oil aspiration pneumonia Early involvement manifests itself as an increase in the bronchial markings, usually on the right These linear striations are often interpreted as bronchiectasis The periphery of the lung is not involved Later the shadows may become confluent and nodular, and they may have an irregular border which suggests the infiltrating nature of a malignancy (Fig 1) The hilar shadows may or may not be en-

larged on the side of involvement Parafinomas may occur forming a large oval mass of smooth outline usually located close to the hilar region

The single most important factor in the x-ray diagnosis of this disease is the persistent nature of the lesions Although the findings in the lung fields may be altered for brief periods by superimposed pulmonary infections, the underlying disease is always present and seen in interim films even though the patient may appear clinically asymptomatic at that time The chief findings may show some progression even though the administration of oily substances is stopped (as in Case IV) This is probably due either to continued superimposed low grade infections at the site of involvement or to the proliferative nature of the disease

X-ray findings are not specific and may be mistaken for bronchiectasis, tuberculosis, silicosis, broncholitis obliterans, and a host of other conditions It is necessary to correlate the history, clinical findings, and chest plate in order to arrive at an early correct diagnosis

### *Pathological Findings*

The gross and microscopic pathological findings are characteristic in lipoid pneumonia, but vary due to the nature of the lipoid aspirated, the amount present in the lungs, and the length of time it has acted upon the lung tissue The term "lipoid pneumonia" is used in this paper because it has become well established by long usage, actually it is a misnomer and the suggested names, such as pneumolipoidosis,<sup>1</sup> are far more descriptive The victims of this disease die from a pneumonia or pneumonitis, the lipoid reaction merely acts as a fertile background and constant and irrevocable predisposing factor

Grossly the lungs are vaguely nodular and on section present rubbery nodules of varying diameters, which in addition to their typical elasticity, have a rather uncommon gray-yellow or gray-brown coloration which is poorly outlined and does not resemble any other process In two of the cases presented lipoid pneumonia was diagnosed from the gross cut sections of the lung prior to verification by microscopic study

Microscopically the mineral oil droplets are absorbed by macrophages which may fill the alveoli and produce a foamy appearance (Fig 2) If the affair is of long standing or the oil is less bland, some fibrous tissue reaction results but in many instances the alveolar walls appear essentially normal and are unaffected by their contents In Case III the mineral oil has served in part as a vehicle for phenolphthalein, a drug whose cathartic action depends on its irritative effect on the bowel mucosa In this case

the connective tissue reaction is far more intense with a chronic inflammatory affair associated with masses of lymphocytes and giant cells forming about the oil droplets. To our knowledge the baleful effect of combinations of oil and phenolphthalein, when introduced into the lung, has not been previously described.

### *Treatment*

The treatment of lipoid pneumonia is entirely prophylactic. It seems apparent from this study that oily medications are contraindicated in neuropsychiatric and debilitated patients. This is unequivocal in any patient with bulbar involvement. Substitution of non-oily laxatives for mineral oil should be easily accomplished with the wide field of laxatives from which to choose. Fat-soluble vitamins are better given in capsule form to these patients. It must be pointed out that mineral and animal oils in the lungs are not absorbed and despite discontinuance of the oil the clinical and x-ray findings will persist and in some instances progress as illustrated in Case III.

### SUMMARY

1) Four cases of lipoid pneumonia in neuropsychiatric and debilitated patients are presented which represented 5.4 per cent in a series of seventy-three autopsies.

2) The diagnosis is based upon a history of ingestion of oily substances, repeated bouts of pneumonia, the demonstration of oily droplets in the sputum following a lipoid-free diet, and the x-ray findings.

3) The x-ray findings are not specific but they are characteristic in the sense that they are persistent even though the patient may be asymptomatic.

4) Pathologically the gross appearance of the lungs is highly suggestive and the microscopic findings are specific.

5) A particularly destructive type of lipoid pneumonia is demonstrated when the mineral oil is employed as a vehicle for phenolphthalein.

6) Treatment consists primarily in prophylaxis.

### RESUMEN

1) Se presentan cuatro casos de neumonía lipoidea en pacientes neuropsiquiátricos y debilitados, que representan el 5.4 por ciento de una serie de setenta y tres autopsias.

2) Se basó el diagnóstico en la historia de la ingestión de sustancias aceitosas, repetidos ataques de neumonía, la demostración de gotitas de aceite en el esputo subsiguiente a una dieta libre de lípidos y los hallazgos radiográficos.

3) Los hallazgos radiograficos no son específicos, pero son característicos en el sentido de que persisten aunque el paciente no tenga síntomas

4) Patologicamente el aspecto macroscópico de los pulmones es muy sugestivo y los hallazgos microscópicos son específicos

5) Se demuestra un tipo de neumonía lipoidea particularmente destructiva que resulta cuando se emplea el aceite mineral como vehículo de la fenoltalina

6) El tratamiento consiste principalmente de la profilaxia

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# Mediastinal Tumors and Cysts

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Indianapolis, Indiana

From a rather extensive review of the literature<sup>1 2</sup> and an analysis of the case records of patients subjected to operation for mediastinal tumors and cysts the following particular impressions were gained

These neoplasms are relatively infrequent The most common primary types are those of the thymus and those arising from lymphatic tissues, dermoids and teratomas, and the neurogenous tumors The cystic dermoids are more frequent than the more solid teratomas Tumors of the sympathetic nerves are the most common type of neurogenous tumors Bronchogenic cysts, fibromas, lipomas and intrathoracic goiters apparently occur somewhat less frequently than the above, while other tumors and cysts of this region seem to be exceedingly rare

The majority of the tumors are malignant and many of the benign ones are potentially malignant It would appear that the majority of the tumors occurring in the mediastinum are those originating from lymphatic tissue and secondary malignant tumors which are not as yet amendable by surgical treatment The other tumors and cysts are principally benign, though a group of primary malignant tumors other than of lymphatic origin occur in this region Primary carcinoma is apparently less frequent than primary sarcoma but secondary sarcoma is rare in the mediastinum Secondary carcinomas in the mediastinum occur most frequently from primary tumors elsewhere in the chest

The majority of thymic tumors are malignant, while many of the benign types, as well as an occasional malignant one, are associated with myasthenia gravis The incidence of malignant tumors is estimated to be between 10 and 20 per cent in neurogenous tumors as well as in dermoids and teratomas The incidence is higher in the more solid teratomas than in the more cystic dermoids A somewhat higher frequency of malignant degeneration is thought to occur in fibromas and malignant degeneration is noted in other tumors of connective tissue A malignant change in cysts other than dermoids would appear to be unusual but is occasionally noted in intrathoracic goiter (about 2 per cent)

Small cell lymphosarcomas and gastro-enterogenous cysts occur clinically, as a rule, in infants and young children while malignant neurogenous tumors, lymphangiomas and bronchogenic cysts are

usually noted before the age of 20 years. Dermoid cysts and teratomas, though often noted in the above age group, are most frequently observed between the ages of 20 and 40, as are benign thymic tumors, benign neurogenous tumors, most benign tumors of connective tissue, intrathoracic goiters, parathyroid adenomas, malignant tumors of lymphatic tissue, sarcomas of the thymus, and other sarcomas. Fibromas, carcinomas of the thymus, and other carcinomas are usually seen after the age of 40 years. The majority of mediastinal tumors and cysts apparently occur before middle age and many are congenital.

Malignant thymic tumors, large cell lymphosarcomas and Hodgkin's disease apparently occur somewhat more frequently in males, while neurofibromas, intrathoracic goiters, and parathyroid adenomas are noted more often in females. There appears to be no particular sex predilection in the other tumors and cysts that is discernable as yet.

There are some signs and symptoms which, if present, are suggestive of the type of tumor and cyst, such as those of myasthenia gravis in benign thymomas, and the marked respiratory distress in the presence of malignant thymic tumors or intrathoracic goiters, and the progressive involvement of nearly all the mediastinal structures and lymphatic tissues in lymphoblastomas. Other symptoms and signs that may indicate the type of tumor are those of nerve involvement, usually before other symptoms are prominent, in neurogenous tumors, the insidious onset with episodes of symptoms, expectoration of hair or sebaceous material in dermoid cysts, as well as symptoms of suppuration in these and bronchogenic cysts. Skin ulceration and activity of the drainage, or associated abdominal symptoms may be noted in gastro-enterogenous cysts. The expectoration of hooklets and scolices as well as the use of indicative tests may be of aid in the diagnosis of echinococcic cysts. Other suggestive symptoms and signs are the apparent external thoracic cage deformity in cartilaginous tumors, and those of hyperthyroidism with a palpable rising nodular mass on swallowing or coughing in intrathoracic goiter. Benign neurogenous tumors, aberrant bronchogenic cysts, pericardial coelomic cysts, fibromas, and those located in the posterior mediastinum are apt to be fairly "silent." In malignant tumors the symptoms are usually progressive and more severe with involvement of the mediastinal structures, and metastasis may be present. Symptoms of long duration are more suggestive of benign tumors. The symptoms in general appear to depend on the location, size and character of the tumor. There may be general signs and symptoms of mediastinal compression and those of implication of specific structures.

Thymic tumors, tumors of lymphatic origin, dermoids and teratomas, pericardial coelomic cysts, lymphangiomas, and apparently fibromas are usually located in the anterior mediastinum. Neurogenous tumors, xanthomas, gastro-enterogenous cysts, and echinococcic cysts are usually noted in the posterior mediastinum. Bronchogenic cysts, hemangiomas, cartilaginous tumors, lipomas, and fibromas, however, may be found anywhere in the mediastinum. Bronchogenic and gastro-enterogenous cysts are frequently located in the right side of the mediastinum. Apparently bronchogenic cysts, tumors of lymphatic tissue, and secondary malignant tumors are frequently seen near the central mediastinum on roentgenograms made of the lateral view of this region.

Certain roentgenologic findings other than the location of the neoplasm, when present, are also suggestive of the type of tumor, such as a flattened disc on the lateral roentgenogram in the case of thymic tumors. Irregular, poorly defined, lobulated borders are usually noted in malignant tumors of lymphatic tissues, though the mass may be somewhat more defined in Hodgkin's disease. Bony erosion of the vertebrae and adjacent ribs may be seen in the presence of benign neurogenous tumors. A smooth, rounded density or the presence of air and a fluid level usually indicates a cyst, while the line formed by two fluids of different density suggests a dermoid cyst. A well-defined lobulated mass which may contain tooth buds frequently denotes a teratoma, while multiple shadows in a circumscribed density suggests a hemangioma or lymphangioma. A lessened peripheral density may indicate a lipoma, while attachment of a mass to skeletal structures is suggestive of cartilaginous and bony tumors. A high wedge-shaped mass, particularly one showing movement on swallowing, is often observed in intrathoracic goiter. A well-defined, smooth, rounded density is suggestive of benign tumor or cyst but a malignant tumor may also present this characteristic. A diffuse, irregular shadow, especially with evidence of bony destruction of the infiltrative type, is suggestive of a malignant tumor. Some benign tumors may simulate this picture, particularly if a complicating infection is present, or may even be hidden by such a condition. The determination of the presence of a mediastinal mass, where possible, is aided by the use of special views and roentgenologic techniques, including the use of contrast media to gain the relationship of structures. Roentgen therapy except as a diagnostic measure where a lymphoblastoma is suspected and as a palliative measure, appears to be of little value.

Broncho-esophagoscopy, in most instances, is of little direct diagnostic value except by inference in the case of mediastinal tumors and cysts but is a definite aid in the differential diagnosis

of many other intrathoracic lesions Exploratory thoracotomy appears to be usually preferable to pneumothorax and thoracoscopy as a diagnostic measure This is because of the dangers and complications of the latter procedure, particularly if adhesions are present, moreover the results are not conclusive in most instances nor is the pneumothorax of much compensatory value With modern methods of anesthesia, the danger of thoracotomy alone is minimal and an operable tumor can be removed at the same time Needle aspiration for biopsy purposes in the case of mediastinal neoplasms holds considerable danger because of the proximity of vital organs If used, it should be reserved for lesions in which there is a question of operability and where the neoplasms are adherent to the chest wall Material for biopsy otherwise can be obtained from those few mediastinal tumors which present themselves in the chest wall or from an external metastasis

It would seem that practically any tumor or cyst in the mediastinum should be explored and the neoplasm removed if possible providing there is no metastasis, irremovable invasion, lymphoblastoma or secondary malignant tumor, and the patient's condition permits operation Surgery is indicated on account of the doubt in many instances as to the character of the neoplasm and because of the incidence of malignant types present within the mediastinum or thorax Operation is also indicated because of the frequent growth of these neoplasms with consequent symptoms and because of the frequency of associated infection with its complications The primary consideration would appear to be whether the intrathoracic tumor were excisable or not Large tumors as such should not deter attempted removal, though some cases present the problems of rapid postoperative adjustment of the cardio-respiratory function following removal inasmuch as gradual compensation of function occurs during the growth of such neoplasms The surgical approach is governed to a large extent by the location and size of the neoplasm Such routes as the sternal-splitting procedure for tumors of the thymus may be used to advantage in some cases Variances of the posterolateral incision and a transpleural approach through the rib bed, however, apparently offer greater accessibility and are satisfactory in most instances In this case, measures must be taken to prevent tension pneumothorax and to bring about expansion of the lung with obliteration of the pleural space (to prevent infection) in the immediate postoperative period This may be accomplished either by drainage or aspiration as indicated

The overall mortality of patients subjected to operation in the past is estimated to be about 30 per cent A fair proportion of the

cases forming the basis of the above estimate were operated on before the period of rapid progress in thoracic surgery. The operative mortality is lower for some neoplasms, even less than 5 per cent, particularly in benign tumors and cysts, with the exception of the gastro-enterogenous group. The direct operative mortality has been considerably reduced in recent years. The majority of deaths occur in those with malignant tumors and where complications, particularly infection, are present. The results are also much better when it is possible to carry out a primary excision of the tumor or cyst. Better management of these cases in recent years is indicated not only by the results, but by the decrease in the hospitalization period required and the decrease in the duration of symptoms of those admitted for operation. There is some evidence that wider use of roentgenologic surveys of the chest may bring about earlier diagnosis—before complications occur—with resultant improved results from surgical treatment.

### RESUMEN

Mediante ciertas observaciones se puede obtener alguna indicación acerca del tipo y carácter de los tumores mediastínicos que ocurren clínicamente. Se ha demostrado que la relativa frecuencia en la ocurrencia de los diferentes neoplasmas junto con la edad cuando aparecen clínicamente, el sexo del paciente y la particular ubicación en el mediastino, tienen algún significado. Se notan algunos signos y síntomas y algunas características roentgenológicas que pueden ser sugestivas. Ocasionalmente se puede obtener tejido de una lesión o metástasis externa para hacer un examen biopsico.

Debido a la frecuencia con que existe duda acerca del carácter del neoplasma en casos que al fin y al cabo desarrollan síntomas debidos a malignidad, crecimiento del tumor e infección, parecería que en la mayor parte de los casos se deben explorar y extirpar los tumores o quistes del mediastino cuando lo sea posible, con tal de que no haya signos de metástasis, invasión no extirpable, linfoblastoma o tumor maligno secundario, y si la condición del paciente permite la intervención quirúrgica.

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## Summary of Talk on Minimal Tuberculous Lesions

Given at the Annual Meeting of the American College of  
Chest Physicians, Chicago, Illinois, June 20, 1948

The Chairman, Francis J Weber, M.D , F C C P , introduced the subject by setting forth the following points

All nations of the world have in the course of history suffered the ravages of tuberculosis Today, in many nations, this disease still attains epidemic proportions In the United States, however, certain forces have joined to bring about a gradual reduction in the death rate What these forces have been, and what their respective roles have been in the reduction of tuberculosis mortality are difficult to assess We may, perhaps, say that the improvement of social and economic conditions has played a part in the process, as well as improvements in medical practice Despite our fortuitous situation, however, we cannot be content when tuberculosis still kills about 50,000 Americans every year, and when it may continue to kill countless thousands in years to come

Epidemiologists, clinicians and public health administrators are vitally concerned with meeting this problem and with preventing most, if not all, of these deaths All who have studied the problem agree that this can best be accomplished through the early discovery of tuberculosis and the prosecution of similar measures which will make control possible Early discovery, we are told, can do two things first, render the individual's prognosis more favorable, and second, through prompt treatment and isolation of infectious cases, prevent spread of the disease to others

With this introduction, the Panel consisting of an impromptu group of Fellows of the College discussed the subject as follows

We are experiencing success in finding the minimal cases The x-ray, which is our principal means of detecting cases of tuberculosis, is finding about seventy per cent of them in a minimal stage However, the discovery of the minimal case engenders many problems, especially in reference to follow-up

Unlike the moderately and far-advanced cases found in surveys, almost all of which have symptoms, the minimal case is very frequently symptom-free When discovered, these cases pose two problems that of activity and that of the method of follow-up

Because the minimal case is so often symptomless, even in those cases later proved active, final diagnosis must rely heavily upon bacteriological findings Where an occasional positive fasting gastric specimen is the only evidence of activity, it should be

confirmed for virulence by injection into guinea pigs. Generally, the "Guide for Disposition of Persons with Abnormal Pulmonary Findings on X-ray Films," published in Public Health Reports, Tuberculosis Control Issue No 10, is a sound guide to the necessary follow-up.

In treatment, there is no doubt that a large-scale trial on the efficacy of streptomycin in minimal lesions is positively indicated and should prove to be highly valuable. For the purpose of facilitating such critical evaluation, in addition to the improvement of diagnostic work in minimal tuberculosis, laboratory facilities should be promoted, increased in number, and improved in the quality of service. The facilities of the Public Health Service's Atlanta Evaluation Laboratory have been organized to give direct service to localities both in consultation regarding technical problems and in the training of both physicians and laboratory workers in bacteriological science and technique.

In the follow-up of minimal tuberculosis, private and general hospitals can serve a vital function. Their active enlistment in the follow-up program should therefore receive serious consideration.

It is well recognized that the clinical management of minimal tuberculosis will vary with the circumstances of the patient and depend upon the facilities available. At the very least, therefore, rest in bed is indicated for active cases of minimal tuberculosis in order to observe progress more closely.

Finally, it should be acknowledged that the tuberculin test, contrary to the belief tenaciously held until recently, is still an extremely valuable guidepost in the diagnosis of tuberculosis. Its use in the evaluation of minimal lesions must therefore be considered a vital part of the follow-up process along with the serial x-ray and bacteriological examinations.

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# EDITORIAL

## FIFTEENTH ANNUAL MEETING, AMERICAN COLLEGE OF CHEST PHYSICIANS

The Fifteenth Annual Meeting of the American College of Chest Physicians will be held in Atlantic City, June 2 through 5, 1949, under the Presidency of Dr Richard H Overholt Those who have attended the past meetings know of the enthusiasm and interest which characterize these active meetings Study of the preliminary program published in this issue of the journal of Diseases of the Chest will reveal that the high standards of the past programs have been maintained in both subject matter and participants Popular features of the previous programs such as the round table luncheons will be repeated, while new features have been added

In general, the subject matter has been arranged under broad classifications, for example, the surgical session will be held Sunday afternoon while principal discussion of chemotherapy will be Friday morning The always popular x-ray conference will be held Saturday afternoon under the direction of Dr M C Sosman of Boston A new feature of the program will be a motion picture session Friday evening, June 3 A group of films will be shown dealing with the many phases of diseases of the chest

Of special interest will be a ten minute resume of the outstanding work of the year in each of the various sub-specialties of diseases of the chest The resumes will be given by a leader in each field to briefly cover points of major interest as well as the advances made in his field during the past year

The program committee has been fortunate in having an unusually wide variety of subjects to choose from in preparing the present program This is due to the scientific interest and investigative spirit of the members of the College and review of the program will give evidence of this clinical and research activity

This year's program has been integrated with that of the Section on Diseases of the Chest of the American Medical Association through the cooperation of its chairman, Major General S U Marietta, and its Secretary, Dr Jay Arthur Myers Members of the College are urged to remain in Atlantic City for the inaugural session of the new Section on Diseases of the Chest and to view the exhibits being prepared for this new Section

I would like to take this opportunity to thank the members of the program committee, namely, Drs Edgar Davis, Juan R Herradora, Edwin R Levine, Herman J Moersch, Leo G Rigler and Harold G Trimble, for their fine cooperation in preparing the annual program of the College

Paul H Holinger, M.D., Chairman,  
Committee on Scientific Program



# Fifteenth Annual Meeting of the College

Ambassador Hotel, Atlantic City, New Jersey

June 2 through 5, 1949

Annual Meeting, American Medical Association

Atlantic City, June 6 through 10, 1949

The College will return this year to the Ambassador Hotel in Atlantic City for the Fifteenth Annual Meeting. In 1947 the College held one of its most successful meetings at the same hotel in Atlantic City and it is anticipated that the 1949 session will be equally successful.

If you are planning to attend the meeting it is **EXTREMELY URGENT** that you make your hotel reservations **IMMEDIATELY**. Some of the hotels in Atlantic City have already announced that they are booked to capacity for the dates of the meetings. A convenient form for hotel reservations appears on page vi of this issue of the journal and if you will complete this form and send it to the Executive Offices of the College in Chicago at once, reservations will be made for you in Atlantic City, if possible, at the Ambassador Hotel.

The Committee on Scientific Program of the College, under the chairmanship of Dr. Paul H. Holinger of Chicago, has announced that the program for the 1949 annual meeting is just about completed. The following are some of the papers which will be presented:

"Significance of Positive Cultures,"

I. D. Bobrowitz, M.D., F.C.C.P., Otisville, New York

"Use of Dihydrostreptomycin in the Treatment of Tuberculosis,"

David T. Carr, M.D., H. C. Hinshaw, M.D., Karl H. Pfuetze, M.D., F.C.C.P. and H. A. Brown, M.D., Rochester, Minnesota

"Angiopneumography,"

Lopo de Carvalho, M.D., F.C.C.P., Lisbon, Portugal

"The Surgical Treatment of Spontaneous Pneumothorax,"

Gerald L. Crenshaw, M.D., F.C.C.P., Oakland, California

"The Regeneration of Defects of the Trachea and Bronchi  
An Experimental Study,"

Rollin A. Daniel Jr., M.D., Nashville, Tennessee

"Pulmonary Aspects of Cystic Fibrosis of the Pancreas,"

Lloyd B. Dickey, M.D., F.C.C.P., San Francisco, California

"Pulmonary Edema,"

Robert M. Eaton, M.D., Grand Rapids, Michigan

"Thirty Years of Artificial Pneumothorax,"

Peter W. Edwards, M.D., F.C.C.P., Shropshire, England

"Histoplasmosis,"

Michael L. Furcolow, M.D., Kansas City, Kansas

"Streptomycin in the Treatment of Miliary and Meningeal Tuberculosis,"

Arnold Shamaskin, M.D., F.C.C.P., Eugene J. Des Autels, M.D., F.C.C.P. and Henry C. Sweany, M.D., F.C.C.P., Hines, Illinois

"Surgical Aspects of Pulmonary Calcification,"

Alfred Goldman, M.D., F.C.C.P., Beverly Hills, California

"The Clinical Evaluation of Disability in Anthracosilicosis,"

Peter A. Theodos, M.D., F.C.C.P., Burgess Gordon, M.D., F.C.C.P., Leonard P. Lang, M.D. and Hurley L. Motley, M.D., Philadelphia, Pennsylvania

- "Experiences in Cardiac Valve Surgery,"  
Dwight Emary Harken, M.D., Boston, Massachusetts
- 'Bronchial Obstruction,"  
Chevalier Jackson, M.D., Philadelphia, Pennsylvania
- "Surgical Management of Lung Abscess,"  
Roy G. Klepser, M.D., Washington, D. C.
- "Cavernostomy,"  
Gustav Maurer, M.D., F.C.C.P., Davos, Switzerland
- 'Carcinoma of the Lung, Its Diagnosis by Cytologic Examination of Sputum and Bronchial Secretions,"  
John R. McDonald, M.D., Rochester, Minnesota
- 'Pulmonary Fibrosis,"  
J. Winthrop Peabody, M.D., F.C.C.P. and J. Winthrop Peabody Jr., M.D., Washington, D. C., Edward W. Hayes, M.D., F.C.C.P., and Edward W. Hayes Jr., M.D., Monrovia, California
- "Residual Lesions in Pulmonary Coccidioidomycosis,"  
H. E. Bass, M.D., F.C.C.P., A. Schomer, M.D., and R. Berke, M.D., New York, New York
- "Preliminary Report on the Use of Para Aminosalicyclic Acid in Pulmonary Tuberculosis,"  
Henry C. Sweany, M.D., F.C.C.P., Chicago, Illinois
- "The Diagnosis of Congenital Malformations of the Cyanotic Type Amenable to Surgery,"  
Helen B. Taussig, M.D., Baltimore, Maryland

## Round Table Luncheon Meetings

A series of round table luncheon meetings will be held on Friday, Saturday and Sunday, June 3, 4 and 5, at the Ambassador Hotel during the annual meeting of the College. Below are listed some of the subjects and moderators for these meetings:

- Suppurative Diseases of the Lungs Dr. Evarts A. Graham, St. Louis, Mo.  
Handling of the Minimal Case Dr. Peter W. Edwards, Shropshire, England  
'Pneumoperitoneum' Dr. Andrew L. Banyai, Milwaukee, Wis.  
'Inhalational Therapy' Dr. Alvan L. Barach, New York, N. Y.  
Status of Pulmonary Resection Dr. Richard H. Overholt, Brookline, Mass.  
Atypical Pneumonias Dr. Italo Volini, Chicago, Ill.  
B. C. G. Dr. Robert J. Anderson, Washington, D. C.  
Bronchial Asthma 'Dr. Maurice Segal, Boston, Mass.  
Dust Diseases 'Dr. Oscar Sander, Milwaukee, Wis.  
'Emphysema and Pulmonary Disability' Dr. Edwin R. Levine, Chicago, Ill.  
'Treatment of Tuberculosis in the Aged' Dr. Harold W. Kohl, Tucson, Ariz.  
'When Should Pneumothorax be Terminated' Dr. Harold G. Trumble, Oakland, Calif.  
'Tuberculosis in Children' Dr. W. L. Howard, Northville, Mich.  
Dosage of New Chemicals and Antibiotics Dr. Karl H. Pfuetze, Cannon Falls, Minn.

Other subjects to be discussed at the round table luncheon meetings are 'Fungus Diseases,' 'Chronic Cor Pulmonale in Pulmonary Diseases,' 'Bronchogenic Carcinoma,' and 'Boeck's Sarcoid.'

The Program Committee appreciates the interest shown by the membership of the College in making suggestions for subjects and moderators for the round table discussions. The suggestions received by the committee were compiled and chosen to meet the popular demand.

## Ten - Minute Resumes

One of the new features in the annual program this year will be a ten-minute resume at the close of each scientific session on an important phase of the specialty of diseases of the chest. The following physicians have accepted invitations to present such resumes at the annual meeting: Dr J Burns Amberson, "Medical Aspects of Diseases of the Chest", Dr Alvan L Barach, "Respiratory Physiology", Dr Brian B Blades, "Surgery", Dr Louis Clerf, "Bronchoesophagology", and Dr M C Sosman, "Roentgenology".

## Luncheon Conferences

### *Annual Conference of College Chapter Officials*

The Annual Conference of College Chapter Officials will hold a luncheon meeting at the Ambassador Hotel on Thursday noon, June 2. Dr Charles A Thomas, Tucson, Arizona, is Chairman of the Conference and Dr Irving Willner, Newark, New Jersey, is Secretary. Problems of interest to the College Chapters, as well as future activities of the Chapters, will be discussed at the meeting.

### *Council on International Affairs*

The Council on International Affairs of the College will sponsor a luncheon meeting on Friday, June 3, at which time members from other countries will make presentations.

### *Council of Tuberculosis Hospitals*

The Council of Tuberculosis Hospitals will hold a luncheon meeting on Saturday, June 4. The activities of the Council, as well as those of the two committees which serve under the Council, namely, the Committee on Sanatorium Standards and the Committee on Rehabilitation, will be discussed at this meeting. Dr Russell S Anderson, Erie, Pennsylvania, Chairman of the Council, will preside at this luncheon meeting.

### *Medical Education*

A luncheon meeting on the subject of medical education will be held on Sunday, June 5, to be presided over by Major General S U Marietta, Washington, D C. The meeting will be addressed by Dr James E Paullin, Professor of Clinical Medicine at Emory University Division, Grady Hospital, Atlanta, Georgia, and Brigadier General George E Armstrong, Deputy Surgeon General, Department of the Army.

## X-Ray Conference

An X-ray Conference will be presented on Saturday afternoon, June 4, starting at 2 00 p m. Members of the College who are interested in presenting x-ray films at the meeting are requested to send their films together with clinical abstract and laboratory findings of the case to Dr M C Sosman, Peter Bent Brigham Hospital, Boston 15, Massachusetts, for consideration. Dr Sosman will serve as Chairman of the X-ray Conference.

## Motion Picture Session

On Friday evening, June 3, a motion picture session will be held at the Ambassador Hotel. Physicians who have interesting motion pictures which they would like to present at this session are invited to make application to Dr. Paul H. Holinger, Chairman, Committee on Scientific Program, American College of Chest Physicians, 500 North Dearborn St., Chicago, Illinois. Applications should include the title of the film, author, approximate running time, whether silent or sound, color or black and white, and the size of the film.

## Fellowship Examinations

Oral and written examinations for Fellowship in the College will be conducted at the Ambassador Hotel on Thursday, June 2. Candidates for Fellowship in the College who are eligible to take the examinations should contact the Executive Secretary, American College of Chest Physicians, 500 North Dearborn Street, Chicago, Illinois.

## Administrative Session

The Administrative Session of the College will be held on Saturday morning, June 4, at which time the Councils and Committees will report. The election of new officers will follow.

## Convocation

The College will conduct a Convocation on Saturday afternoon, June 4, when Fellowship Certificates will be awarded. The Convocation will be conducted by the Board of Regents of the College and a guest speaker will address the assembly.

## Cocktail Party and Presidents' Banquet

The Annual Presidents' Banquet will be held on Saturday night, June 4. Dr. Richard H. Overholt, President of the College, will deliver his presidential address and the President-Elect, Dr. J. C. Placak, will be installed as President. The award of the College Medal will also be made at the banquet. A cocktail party will precede the Annual Presidents' Banquet.

## Board Meetings

The Board of Regents and Board of Governors of the College will hold their annual meetings on Thursday, June 2, in Atlantic City. The College Councils and Committees will also hold meetings at the time of the annual session in Atlantic City.

## Section on Diseases of the Chest

The Section on Diseases of the Chest of the American Medical Association will meet on Wednesday, June 8, and Thursday, June 9, in Atlantic City. There will also be a Section on Diseases of the Chest in the Scientific Exhibits of the American Medical Association at the annual session in Atlantic City.

OFFICIALS OF SOCIETIES PARTICIPATING IN THE VIII CONGRESS OF ULAST, MEXICO CITY, D F



*Left to right* Ismael Cosío Villegas, M.D., FCCP, President of the VIII Congress of ULAST, Mr. Murray Kornfeld, Executive Secretary of the American College of Chest Physicians, Jorge A. Higgins, M.D., FCCP, President-Elect for the IX Congress of ULAST to take place in Guayaquil, Ecuador, in 1951, Richard H. Overholt, M.D., FCCP, President of the American College of Chest Physicians, and Esmond R. Long, M.D., Executive Secretary of the American Trudeau Society

## VIII Congreso Panamericano de Tuberculosis (ULAST) III Congreso Nacional de Tuberculosis y Silicosis

The VIII Congreso Panamericano de Tuberculosis (ULAST) and the III Congreso Nacional de Tuberculosis y Silicosis were held in Mexico City, Mexico, January 23-29. Physicians numbering 262, representing 20 countries, namely, Argentina, Bolivia, Brazil, Canada, Chile, Costa Rica, Cuba, Dominican Republic, Ecuador, France, Guatemala, Italy, Mexico, Republic of Panama, Peru, Philippine Islands, El Salvador, United States of America, Uruguay and Venezuela, registered for the meeting. The scientific sessions were of a very high caliber and were well attended. The sessions were held at the Cardiological Institute in Mexico City, one of the very few institutes of its kind in the world.

The hospitality of the physicians in Mexico could not be surpassed. Entertainment in the form of dinners, receptions and tours were arranged for the physicians and their wives, and on Saturday evening, January 29, a dinner and grand ball were given at the Hotel del Prado. Dr. Ismael Cosío Villegas, President of the VIII Congress of ULAST, and Dr. Alejandro Celis, the President of the III National Congress of Tuberculosis and Silicosis, as well as the other officers of the Congresses, are to be congratulated for the outstanding meeting which they planned and directed.

The following members of the American College of Chest Physicians attended the VIII Pan American Congress of the Union of Latin America Societies of Tuberculosis (ULAST), and the III National Congress of Tuberculosis and Silicosis, which took place in Mexico City, January 23-29, 1949. Of the 262 registrants, 108 were members of the College.

**ARGENTINA** (7) Oscar P. Aguilar, Ovidio Francisco R., Jose Antonio Perez, Gumersindo Sayago, Alberto Jose Soubrie, Raul Vaccarezza, and Jose F. Verna

**BOLIVIA** (1) Enrique Vargas Sivila

**BRAZIL** (2) Jose Silveira, and Valouis Souto

**CANADA** (1) John Carmichael Kovach

**COSTA RICA** (2) Arturo Blanco Solis, and Carlos M. Trejos Flores

**CUBA** (10) Gustavo Aldereguia Lima, Jose Garcia Arruzaria, Juan J. Castillo, Augusto Fernandez Conde, Luis de la Cruz Muñoz, Rafael Meneses Mañas, Rene G. Mendoza, Antonio Navarrete, Ricardo Sanchez Acosta, and Eugenio Torroella M. Fortun

**DOMINICAN REPUBLIC** (1) Juan Moscoso Cordero

**ECUADOR** (2) Armando Pareja Coronel, and Jorge A. Higgins

**EL SALVADOR** (1) Victor Hugo Lucha

**GUATEMALA** (3) Leon Araujo G., Rafael Leal H., and Enrique Coronado Iturbide

**MEXICO** (39) Carlos Aguilar, Donato G. Alarcon, Manuel Alonso, Salvador Gomez Alvarez, Rafael Artasanchez, Felipe Aladro Azueta, Ramon Celis Baltazar, Octavio Bandala, Cesar Becerra, Manuel Beltran del Rio, Jesus M. Benitez, Segundo Braña Blanco, Melchor Colon y Camacho, Santiago Caparrosio Mario Martinez Carrouche, Jose F. Colon, Ismael Cosío Villegas, Leopoldo Castro Fernandez, Pedro Alegria Garza, Rodolfo Gil, Elihu J. Gutierrez, Guillermo Solorzano Gutierrez, Rafael Ibarra Perez, Miguel Jimenez Fernando Katz, Alberto Ladron de Guevara, Vicente A. Moreno, Antenogenes Mundo, Carlos Noble,

## AMERICAN COLLEGE OF CHEST PHYSICIANS

April, 1949



Left to right, 1st row Fernando Gomez, Uruguay, Gumersindo Sayago, Argentina, Esmond Long, United States, Ismael Cosio Villegas, Mexico, Chevalier L. Jackson, United States, Richard H. Overholt, United States —2nd row Murray Kornfeld, United States, Attilio Omodei Zorini, Italy, Ovidio Garcia-Rosell, Peru, Herbert L. Mantz, United States, J. Winthrop Peabody, United States, Jose Antonio Perez, Argentina —3rd row Jose Silveira, Brazil, Horacio Rubio Palacios, Mexico, Manuel Alonso, Mexico, Juan Escudero Villar, Peru, Louis Mark, United States —4th row Juan M. Moscoso Cordero, Dominican Republic, Raul Soules-Baldo, Venezuela, Juan R. Herrera, Argentina —5th row —6th row Marcio Bueno, United States, Robert J. Anderson, United States, Henry C. Sweany, United States, Raul Vaccarezza, Argentina —7th row —8th row Marcio Enrique Coronado Iturbide, Guatemala, Frank S. Dolley, United States, Costa Rica, Santiago Madeiros, Bolivia —9th row —10th row Gustavo Aldereguia, Cuba, Donato G. Alarcon, Mexico, Ricardo Sanchez Acosta, Cuba

J Jesus Olivo, Jose Manuel Ortega, Carlos R Pacheco, Fernando Re-bora, Aradio Lozano Rocha, Ubaldo Roldan, Horacio Rubio Palacios, Alberto Sansom, Enrique Stames Davila, Antonio Rios Vargas

PANAMA (1) Amadeo Vicente Mastellari

PERU (6) Juan Escudero Villar, Max Espinoza Galarza, Ovidio Garcia-Rosell, Juan Macchiavello, Juan A. Werner, and Humberto Valderrama

PHILIPPINES (1) Francisco S Guerrero

UNITED STATES OF AMERICA (21) Robert J Anderson, Oscar Auerbach, Marcio Bueno, Frank S Dolley, Seymour M Farber, Alfred Goldman, Edward A. Greco, Juan R Herradora, Chevalier L Jackson, Edwin R Levine, Herbert L Mantz, Louis Mark, Richard H Overholt, J Winthrop Peabody, Robert A Peers, Arthur Q Penta, G S Pesquera, John Robert Phillips, Henry C Sweany, C A. Thomas, and Leonid Zavatsky

URUGUAY (6) Alejandro A Artagaveytia, Raul Burgos, Cleopatria Epifanio, Fernando D Gomez, Rene Racine, and Juan Soto Blanco

VENEZUELA (4) R Soules-Baldo, Cesar Rodriguez, Julio Rodriguez, and R Soto Matos

## Meeting, Council on Pan American Affairs

On Tuesday morning, January 25, the Council on Pan American Affairs of the American College of Chest Physicians sponsored a breakfast meeting at the Hotel del Prado to which all officers of the College attending the meeting in Mexico City were invited. Dr Chevalier L Jackson, Philadelphia, Chairman of the Council, presided at the meeting and introduced the following officers who presented reports concerning the activities of the College in their countries

ARGENTINA Gumersindo Sayago, M.D., Cordoba, Regent and Past-President, Argentine Chapter, Raul F Vaccarezza, M.D., Buenos Aires, Governor and Past-President, Argentine Chapter, Jose Antonio Perez, M.D., Cordoba

BOLIVIA Santiago Medeiros, M.D., La Paz

BRAZIL Jose Silveira, M.D., Salvador, Bahia, Governor and President, North Brazilian Chapter

COSTA RICA Arturo Blanco Solis, M.D., San Jose, Carlos M Trejos Flores, M.D., San Jose

CUBA Antonio Navarrete, M.D., Havana, Regent, Gustavo Aldereguia, M.D., Havana, Past-President, Cuban Chapter, R Sanchez Acosta, M.D., Havana, Vice-President, Cuban Chapter

DOMINICAN REPUBLIC J M Moscoso Cordero, M.D., Trujillo, Governor

GUATEMALA Enrique Coronado Iturbide, M.D., Guatemala City, Governor

MEXICO Ismael Cosio Villegas, M.D., Mexico City, ULAST President, Governor and President, Mexican Chapter, Donato G Alarcon, M.D., Mexico City, Regent and Past-President, Mexican Chapter, Miguel Jimenez, M.D., Mexico City, Vice-President, Mexican Chapter, Manuel Alonso, M.D., Mexico City, Past-Secretary, Mexican Chapter, Horacio Rubio Palacios, M.D., Mexico City, Secretary, Mexican Chapter

PERU Ovidio Garcia Rosell, M.D., Lima, Regent and Past-President, Peruvian Chapter, Juan Escudero Villar, M.D., Vice-President, Peruvian Chapter, Max Espinoza Galarza, M.D., Lima, Past-President, Peruvian Chapter



URUGUAY Fernando Gomez, M D , Montevideo, Secretary of ULAST and Governor

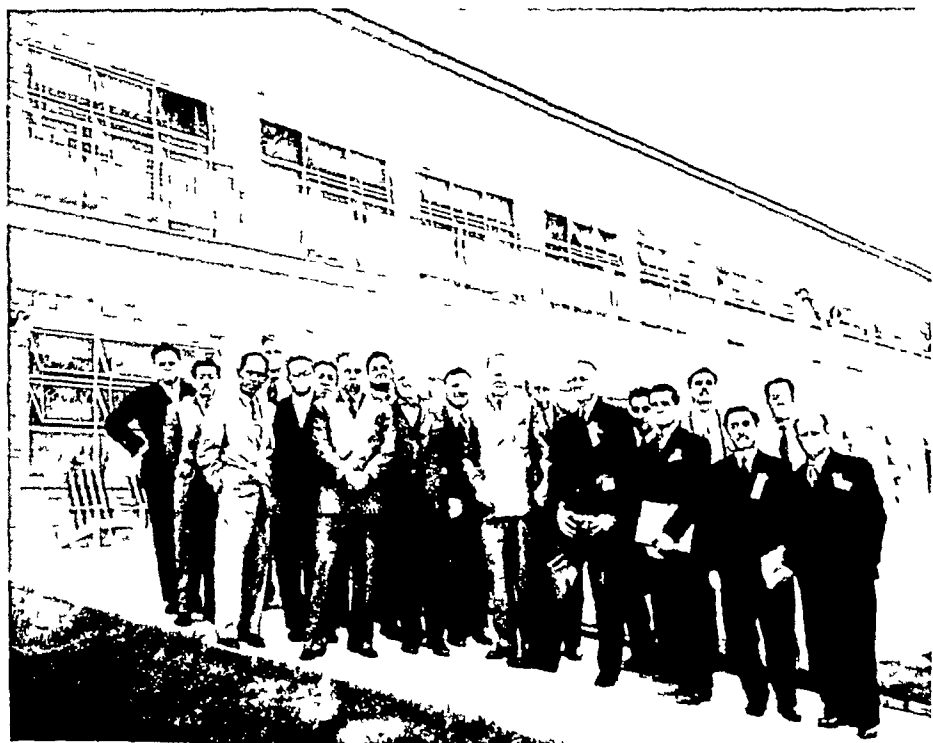
VENEZUELA Raul Soules Baldo, M D , Caracas

UNITED STATES OF AMERICA J Winthrop Peabody, M D , Washington, D C , Past-President and Chairman, Council on Postgraduate Medical Education, Louis Mark, M D , Columbus, Ohio, First Vice-President, Frank S Dolley, M D , Los Angeles, California, Regent, Herbert L Mantz, M D , Kansas City, Missouri, Regent, Juan R Herradora, M D , Jersey City, N J , Secretary, Council on Pan American Affairs, Arthur Q Penta, M D , Schenectady, N Y , member, Council on Pan American Affairs, Henry C Sweany, M D , Chicago, Illinois, member, Council on Pan American Affairs, Robert J Anderson, M D , Washington, D C , Chairman, Council on Public Health, and Murray Kornfeld, Chicago, Illinois, Executive Secretary of the College

The meeting was also addressed by Dr Richard H Overholt, Brookline, Massachusetts, President of the American College of Chest Physicians Dr Esmond R Long, Philadelphia, Pennsylvania, Executive Secretary of the American Trudeau Society and Editor of the American Review of Tuberculosis and Dr Attilio Omodei Zorini, Director of the Forlini Institute, Rome, Italy, were invited guests and addressed the conference

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#### VISITORS TO SANATORIO SAN ANGEL, MEXICO CITY, D F



A group of physicians visiting the Sanatorio San Angel, Mexico, during the VIII Congress of ULAST, at the invitation of Dr Donato G Alarcon, Medical Director

## MEXICAN CHAPTER SPONSORS LUNCHEON MEETING

The Mexican Chapter of the College sponsored a luncheon meeting at the Paolo Restaurant on Thursday, January 27. All members of the American College of Chest Physicians who were in Mexico City for the Congresses were invited to attend this luncheon. A brief address was given by each of the following:

Donato G. Alarcon, M.D., Mexico City,

Regent of the College for Mexico, Presiding

Richard H. Overholt, M.D., Brookline, Massachusetts,

President, American College of Chest Physicians

Chevalier L. Jackson, M.D., Philadelphia, Pennsylvania,

Chairman, Council on Pan American Affairs

Fernando D. Gomez, M.D., Montevideo, Uruguay, Secretary of ULAST,  
and Governor of the College for Uruguay

Mr. Murray Kornfeld, Chicago, Illinois,

Executive Secretary, American College of Chest Physicians

Dr. Manuel Alonso, past secretary of the Mexican Chapter, was introduced and complimented for his efforts in arranging the luncheon meeting. Dr. Horacio Rubio Palacios, the new secretary of the chapter, was also introduced.

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Visitors to the United States of America

Following the meeting of the VIII Pan American Union of Latin American Tuberculosis Societies (ULAST) and the III National Congress of Tuberculosis and Silicosis in Mexico City, a number of College members from various parts of the world visited clinics, hospitals and the Executive Offices of the College during a tour of the United States of America. Some of the members were accompanied by their wives.

## ARGENTINA

From the Argentine came Dr. Raul F. Vaccarezza, Governor of the College for Argentina. Dr. Alberto Jose Soubrie, Mrs. Vaccarezza and Mrs. Soubrie. They flew from Mexico City to Havana, Cuba, and then traveled to New York City via Miami. They were met in New York City by Dr. Juan R. Herradora, Secretary of the Council on Pan American Affairs for the College, and were entertained by Dr. Herradora during their stay in New York City. Drs. Vaccarezza, Soubrie and their wives returned to Buenos Aires via New Orleans.

## BRAZIL

From Brazil came Dr. Jose Silveira, Governor of the College for North Brazil and President of the North Brazilian Chapter of the College. Dr. Silveira visited Los Angeles, San Francisco, Denver, Chicago, Washington, D.C., Philadelphia and New York City. While in Philadelphia, Dr. Silveira attended the postgraduate course in diseases of the chest sponsored by the Pennsylvania Chapter of the College and the Laennec Society of Philadelphia, held at the Warwick Hotel from February 28 through March 4. Dr. Silveira visited the tuberculosis hospitals and clinics in California and in Denver where he delivered a lecture at the

GUESTS OF DR AND MRS JUAN R. HERRADORA, SECRETARY OF THE COUNCIL ON PAN AMERICAN AFFAIRS



*Left to right, standing* Dr Juan R. Herradora, Secretary of the Council on Pan American Affairs, Dr Raul Burgos, Dr Raul Vaccarezza, Dr Fernando D. Gomez, Dr Jose Silveira, Dr Alejandro A. Artagaveytia — *Seated* Mrs Artagaveytia, Mrs Soto Blanco, Mrs Herradora, Mrs Vaccarezza — *On floor* Dr Cleopatria Epifanio, Dr Alberto J. Soubrie and Mrs Soubrie

National Jewish Hospital on "B C G Vaccine in Brazil" In Chicago, Dr Silveira was the guest of honor at a dinner sponsored by the Illinois Chapter of the College at the Congress Hotel on February 11, and he spoke on "The World Organization of the College" While in Chicago, Dr Silveira addressed a staff meeting at the Municipal Tuberculosis Sanitarium on "Pulmonary Schistosomiasis in Brazil" He spent some time at the Executive Offices of the College in Chicago discussing the organization of the College in Brazil In Brazil at the present time there are four College Chapters and the organization of a fifth chapter is contemplated While in the East, Dr Silveira visited the Fall River Tuberculosis Hospital, Fall River, Massachusetts as a guest of Dr Marcio Bueno, where he gave a paper before the hospital staff on "The Advantages of Oral B C G Vaccination"

#### DOMINICAN REPUBLIC

From the Dominican Republic came Dr Juan Moscoso Cordero, Governor of the College for the Dominican Republic Following a brief visit in Los Angeles, Dr Moscoso Cordero visited the Executive Offices of the College in Chicago He then went on to New York City where he spent several weeks visiting hospitals and clinics in the metropolitan district

#### GUATEMALA

From Guatemala came Dr Rafael Leal, President of the Central American Chapter of the College, and Dr Jose Colon These physicians also visited Los Angeles and San Francisco, California

#### ITALY

From Italy came Dr Attilio Omodei Zorini, Director of the Forlanini Institute of Rome He flew from Mexico City to New York City, where he visited Seaview Hospital as the guest of Dr David Ulmar Dr Zorini then flew to Chicago for a visit with Mr Murray Kornfeld, Executive Secretary of the American College of Chest Physicians He was guest of honor at a dinner given at the Palmer House, Chicago, on February 5 Among others, the dinner was attended by Dr and Mrs Juan Escudero Villar, and Dr and Mrs Humberto Valderama, Lima, Peru, Dr Juan Moscoso, Trujillo, Dominican Republic Mrs E W Hayes, Monrovia, California, Dr and Mrs Italo Volini, Dr and Mrs Minas Joannides, Dr and Mrs Edwin R Levine and Dr and Mrs Henry C Sweany, all of Chicago, and Dr James R Perkins Managing Director of the National Tuberculosis Association New York City Mr and Mrs Murray Kornfeld and Miss Harriet Lumm of the Executive Offices of the College also attended the dinner

#### PERU

From Peru came Dr Ovidio Garcia Rosell, Regent of the College, Dr Max Espinoza Galarza, past president of the Peruvian Chapter of the College, and Dr Juan Macchiavello They visited Los Angeles and San Francisco, California Dr Juan Escudero Villar, Vice-President of the Peruvian Chapter and Dr Humberto Valderrama flew direct from Mexico City to Chicago, where they visited a number of hospitals, clinics and the Executive Offices of the College They were guests at a dinner given in their honor at the Palmer House on February 5 They were accompanied by Mrs Escudero Villar and Mrs Valderrama From Chicago

they went to New York City and Washington, D C In New York City they were greeted by Dr Juan R Herradora, Jersey City, New Jersey

#### PHILIPPINE ISLANDS

From the Philippine Islands came Dr Francisco S Guerrero, Chief Surgeon of the Quezon Institute, Manila Dr Guerrero visited a number of hospitals, clinics and the Executive Offices of the College in Chicago as a part of his itinerary, which included visits to a number of medical centers throughout the world Dr Guerrero plans on spending several months in the United States, and will then leave for Europe before returning to the Philippine Islands

#### URUGUAY

From Uruguay came Dr Fernando D Gomez, Governor of the College for Uruguay, Dr Alejandro Artagaveytia, Dr Raul Burgos, Dr Cleopatra Epifanio, Dr Rene Racine and Dr Juan Soto Blanco Mrs Artagaveytia and Mrs Soto Blanco accompanied their husbands to the United States of America They flew from Mexico City to Los Angeles, where they were the guests of Dr Frank S Dolley, Regent of the College for California, Dr Lyman A Brewer, III, Vice-President of the California Chapter of the College and Dr Alfred Goldman While in Los Angeles they visited Olive View Sanatorium, Duarte Sanatorium and the Veterans Hospital at San Fernando They next visited San Francisco where they were the guests of Dr Seymour M Farber, Secretary of the California

#### URUGUAYAN DELEGATION ARRIVES IN CHICAGO, ILLINOIS



*Left to right, top row Dr Rene Racine Dr Alejandro C Artagaveytia, Dr Juan Soto Blanco —Bottom row Dr Raul Burgos Dr Fernando D Gomez Dr Cleopatria Epifanio and an airline hostess for the United Airlines*

Chapter of the College and Dr M A Benioff They then visited Denver, Colorado, where they were greeted by Dr W Bernard Yegge, Secretary of the Rocky Mountain Chapter of the College

The next stop on their itinerary was Chicago, and following a visit to the Executive Offices of the College their stay in Chicago was taken up by visits to the hospitals and clinics They were the guests at the Municipal Tuberculosis Sanitarium of Dr Henry C Sweany, member of the Council on Pan American Affairs of the College and Dr Sol Roy Rosenthal, Director of the Tice BCG Clinic at the Cook County Hospital A dinner was given in their honor at the Hotel Moraine, Highland Park Illinois, on Sunday, February 13 This dinner was also attended by Dr Jose Silveira of Brazil

After leaving Chicago, they flew to Washington, D C, and then on to New York City, where they were greeted and entertained by Dr Juan R Herradora, Secretary of the Council on Pan American Affairs in the College The doctors and their wives were guests of Dr Chevalier L Jackson, Chairman of the Council on Pan American Affairs of the College in Philadelphia on February 28 Enroute from New York City to Uruguay they stopped off at San Juan Puerto Rico where they were guests of the Puerto Rican Chapter of the College Some of the doctors stopped off for brief visits at Trinidad and Rio de Janeiro, while the others proceeded direct to Montevideo Uruguay

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## College Chapter News

### NEW JERSEY CHAPTER

The annual meeting of the New Jersey Chapter will be held at the Ambassador Hotel Atlantic City, in conjunction with the annual meeting of the Medical Society of New Jersey, April 25-28 The chapter will hold a luncheon meeting on April 28 The following scientific program will be presented in the Section on Chest Diseases of the Medical Society of New Jersey

"Experience with Para Amino Salicylic Acid in the Treatment of Tuberculosis,"

Benjamin P Potter, M.D F C C P, Jersey City

Discussant Emanuel Klosk M.D, F C C P, Newark

"Treatment of the Unexpandable Lung,"

Paul Geary, M.D, Scotch Plains

Discussant Philip J Kunderman, M.D, New Brunswick

"Cor Pulmonale, Its Relationship to Pulmonary Disease, Cause and Effect,"

Paul K. Bornstein, M.D F C C P, Asbury Park

Discussant Irving L Applebaum, M.D, F C C P, Newark

"The Second Most Important Silent Lesion,"

Richard H Overholt, M.D, F C C P, Brookline, Massachusetts

Discussant George N J Sommer Jr, M.D, Trenton

Dr Joseph A Smith is Chairman of the Section on Chest Diseases and Dr Juan R Herradora is Secretary Dr Edwin R Levine of Chicago, will present a paper on BCG in the Section on Pediatrics of the Medical Society of New Jersey

## OHIO CHAPTER

The Ohio Chapter of the College will hold its annual meeting in Columbus on April 20, in conjunction with the Ohio State Medical Association meeting, April 19-21. The chapter will hold a luncheon meeting at the Neil House which will be followed by the business meeting. A scientific program as follows will be presented after the business meeting:

"Pneumoperitoneum,"

William J. Habeeb, M.D., F.C.C.P. and  
Howard Reiser, M.D., F.C.C.P., Springfield, Ohio

"Experience with Papanicolaou Technique in the Diagnosis of  
Pulmonary Malignancies,"

Neil Andrews, M.D., F.C.C.P., Walter Baum, M.D., F.C.C.P. and  
Karl P. Klassen, M.D., F.C.C.P., Columbus, Ohio

X-Ray Conference

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## PACIFIC NORTHWEST DISTRICT CHAPTER

The annual meeting of the Pacific Northwest District Chapter of the College was held in Portland, Oregon, Friday and Saturday, November 5 and 6, 1948. Scientific sessions were held in the University of Oregon Medical School Library Auditorium. Dr. Paul Samson of Oakland, California, was guest speaker.

New chapter officers elected at the business meeting were:

W. Elliott Harrison, M.D., Vancouver, B.C., President  
Frederick Slyfield, M.D., Seattle, Washington, Vice-President  
Florence A. Brown, M.D., Portland, Oregon, Secretary-Treasurer

Mrs. William S. Conklin entertained the physicians' wives at tea in her home Friday afternoon.

In the evening an informal banquet at the University Club was attended by wives and guests as well as member physicians, with about seventy persons present. The retiring President, Dr. Grover Bellinger, accorded recognition to the memory of three members lost by death during the past year, namely, Dr. Philipp Schonwald, Seattle, Dr. Leon G. Woodford, Everett, Washington, and Dr. Irvin R. Fox, Eugene, Oregon.

Speaker of the evening was Dr. Howard P. Lewis, Professor and Head of the Department of Medicine, University of Oregon Medical School. He talked on "Some Aspects of Education in Chest Diseases." He stressed, first, the advances made in the treatment of chest diseases in the last two decades, and second, the need for full utilization of physical examination and careful interpretation of positive findings before requesting costly laboratory procedures.

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## WISCONSIN CHAPTER

The Wisconsin Chapter of the College held meetings in Milwaukee on January 28 and on February 25. Dr. Ross Weller presented a talk on "Bacterial Allergy" at the January meeting, and Dr. Mischa Lustok discussed "Myocarditis" at the meeting held in February.

## ILLINOIS CHAPTER

The annual meeting of the Illinois Chapter of the College will be held at the Palmer House, Chicago, on Sunday, May 15, preceding the annual meeting of the Illinois State Medical Society, May 16-18, 1949. The following scientific program will be presented by the chapter commencing at 2 00 p m

"Pulmonary Manifestations of Sarcoidosis,"

Andrew L. Banyai, M.D., F.C.C.P., Milwaukee, Wisconsin

"Cavernostomy in Pulmonary Tuberculosis,"

John V. Thompson, M.D., F.C.C.P., Indianapolis, Indiana

"The Treatment of Chronic Pulmonary Suppurations,"

William M. Tuttle, M.D., Detroit, Michigan

"Decortication of the Lung in the Treatment of Empyema,"

Thomas H. Burford, M.D., St. Louis, Missouri

Subject to be announced,

Leo G. Rigler, M.D., F.C.C.P., Minneapolis, Minnesota

A business meeting will be held following the scientific program. A guest speaker to be announced will address the dinner meeting of the chapter, Sunday night, May 15.

## ARIZONA CHAPTER

The Arizona Chapter will hold its annual meeting in Tucson in conjunction with the annual meeting of the Arizona State Medical Association, May 8-10, 1949. A scientific program on diseases of the chest will be presented at the chapter meeting.

## PUERTO RICO CHAPTER

The Puerto Rico Chapter of the College held its annual meeting on December 11 in conjunction with the annual meeting of the Puerto Rico Medical Association. A business meeting was held in the morning which was followed by a luncheon at the Navy Beach Club, San Juan. After the luncheon the following scientific program was presented:

"Combination Pneumothorax-Pneumoperitoneum in the Therapy of Pulmonary Tuberculosis,"

Jose L. Porrata, M.D., Santurce

"Mixed Bronchial Tumor" (Presentation of a Case),

David Rodriguez Perez, M.D., Rio Piedras

"Tumors of the Lung and Mediastinum" (Presentation of Cases),

Luis A. Passalacqua, M.D., F.C.C.P., Santurce

"Radical Surgery in Extrinsic Cancer of the Larynx" (Preliminary Report),

David Rodriguez Perez, M.D., Rio Piedras, and

Jose Pico, M.D., F.C.C.P., Santurce

The following officers of the chapter were elected for the year 1949:

Dr. Angel M. Marchand, President

Dr. Pedro J. Durand, Vice-President

Dr. Ezequiel Martinez Rivera, Secretary-Treasurer

Dr. Hector Marrero Otero, Dr. Juan H. Font, and

Dr. Leandro Santos, Board Members



### CALIFORNIA CHAPTER

The annual meeting of the California Chapter of the College will be held in Los Angeles in conjunction with the annual meeting of the California Medical Association, May 8-11, 1949. An interesting program on chest diseases is being prepared for presentation at the meeting.

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### NEW YORK STATE CHAPTER

The New York State Chapter will hold its annual meeting in Buffalo in conjunction with the annual meeting of the Medical Society of the State of New York, May 2-6, 1949. An interesting program will be presented in the Section on Diseases of the Chest in the state medical society.

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### CENTRAL AMERICAN CHAPTER

The Central American Chapter held its II Annual Reunion at the Sanatorio Antituberculoso, Guatemala, on January 19, 1949, in conjunction with the III Central American Congress of Tuberculosis. An excellent scientific program was presented. Amadeo Vicente Mastellari, M.D., F.C.C.P., Republic of Panama, Regent of the College for Central America, was the guest of honor.



Second Annual Meeting of the Central American Chapter of the American College of Chest Physicians, Guatemala, January 19, 1949

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### VIRGINIA CHAPTER

The annual meeting of the Virginia Chapter was held at the Richmond Veterans Administration Hospital on March 1, with Dr. Dean B. Cole, President, presiding. There were 75 physicians in attendance including a large delegation from the Potomac Chapter and other guests from West Virginia and North Carolina. The new officers elected for the chapter are as follows: Dr. E. C. Drash, President, Dr. Kinloch

Nelson, Vice-President, and Dr C W Scott, Secretary-Treasurer The following scientific program was presented

"Recent Advances in Resection and Cavernostomy,"  
J D Murphy, M.D , F C C.P , Oteen, North Carolina

"Pneumoperitoneum,"  
R E Moyer, M.D , F C C.P , Oteen, North Carolina

"Laboratory Aids in Fungus Diseases,"  
Abraham Rosensweig, Ph.D , Richmond, Virginia

"Bronchogenic Carcinoma,"  
Paul Kriz, M.D , Richmond, Virginia

"Blastomycosis,"  
J P Williams, M.D , Richmond, Virginia

The next meeting of the Virginia Chapter will be held at the Chamberlayne Hotel, Old Point Comfort, Virginia, during the meeting of the state medical society, May 2 to 5, 1949

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## College News Notes

Dr Francis L Lederer, Professor and Head of the Department of Otolaryngology, University of Illinois College of Medicine, recently conducted a survey of hearing and speech needs in Mexico, at the invitation of the Under-Secretary of Health and Welfare of Mexico Dr Lederer also participated in the first postgraduate course in otolaryngology offered by the University of Mexico Medical School

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Dr Ralph H Homan, El Paso Texas, has been elected President-Elect of the El Paso County Medical Society

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Dr John S Harter, Louisville, Kentucky, has accepted an invitation to participate in the 1949 session of the Texas State Medical Association which is to be held in San Antonio, May 3-5

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Dr Eli H Rubin New York City, has been named director of medicine and chairman of the medical staff at Seton Hospital in the Bronx a 500 bed tuberculosis institution taken over by the city last May

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Dr George W Waldron, Houston Texas has been elected President-Elect of the Harris County Medical Society

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## Obituaries

GEORGE CHAMBERS ANGLIN

1890 - 1948

Following a full day's Medical duties on Tuesday April 16th, 1948, Dr Anglin suffered an almost immediately fatal heart seizure during that night

Born in Ireland, Dr Anglin came to Canada in 1907 and graduated from the University of Toronto in 1914 He served in the R.A.M.C from

1915 to 1918 He continued as Director of the Chest Clinic at Christie Street Military Hospital and during the Second World War, was Chest Consultant for the three services in the Toronto Military District For his services in the same capacity to the Norwegian Air Force he was signally honored by the King of Norway

He was a member of the Staff of the Toronto Western Hospital and enjoyed a large consulting practice in allergic and chest diseases His interests were international In addition to his Canadian affiliations he was a member of many other medical bodies including the American College of Physicians, the Trudeau Society, American Academy of Allergists and the American Board of Internal Medicine He was one of the early Canadian Fellows of the American College of Chest Physicians and active in promoting its interests He was a member of the Senate of the University of Toronto from 1944, President of the Medical Alumni Association of the University in 1945-46 and included amongst his activities those of the Church and Philanthropic bodies

The profession in Canada has suffered a severe loss in his untimely death

H I Kinsey, Governor for Ontario

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### IRVIN REGINALD FOX

1891 - 1948

With the passing of Dr Irvin Reginald Fox of Eugene, Oregon, on September 21, 1948, the community and the medical profession suffered a severe loss He was an indefatigable, conscientious worker, a keen thinker and able diagnostician None, either the rich or poor, the distinguished or unknown, were denied his services, and his humanitarian attitude won him many friends among the laity Knowing that the end was near unless he rested from his exacting duties, his only thought was the comfort and the welfare of his patients which led directly to his untimely death All who had the privilege of knowing Dr Fox will miss his friendly smile and counsel

His practice was limited to Internal Medicine but his main interest was diseases of the chest, especially cardiology and tuberculosis

He was a Fellow of the American College of Chest Physicians, a Fellow of the American College of Physicians and a member of the American Thoracic Association, a member of his County Medical Society, of the Oregon State Medical Society and a member of the American Medical Association He was formerly Chief of Staff of the Sacred Heart Hospital in Eugene, Oregon and a member of the Medical Examining Board of the State of Oregon and its former president At the time of his death, he was Chief of the Medical Section of the Staff of the Sacred Heart Hospital in Eugene, Oregon

He was born in Oregon City, Oregon, on January 25, 1891 He was graduated from the University of Oregon in 1917 and the University of Oregon Medical College in 1921 Shortly after that, he located in Eugene and held a residency in medicine He married Edyl Fraasch in 1917 and she bore him along with two children

J M Odell, M D, Governor for Oregon

# DISEASES *of the* CHEST

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## Undergraduate and Postgraduate Teaching in Diseases of the Chest

*A Report of the Joint Program of the New York Medical College\*  
and the  
Municipal Tuberculosis Sanatorium of the City of New York*

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New York, New York

Tuberculosis is an endemic disease that constantly presents the threat of increasing to epidemic proportions. The aftermath of war has amply demonstrated how that threat can become an actuality. The tremendous optimism that tuberculosis had at last reached a stage where control could be logically and rationally envisioned faded rapidly before the realities of destruction, displacement and deprivation. Again available forces have been marshalled to control the disease. Mass x-ray surveys, national and international Public Health Commissions, antibiotics—all are part of the armamentarium. The vast program can succeed only if adequately trained and sufficient personnel is available to administer it. The disease must be recognized early and facilities be made available for treatment. The bulwark of this program must be the physician upon whose training and skill the plan must stand or fall. It is not sufficient to have a trained body of specialists in tuberculosis. It would be almost impossible to obtain a sufficiently large number of such men. They must be the nucleus but they cannot possibly hope to cope with so gigantic a problem without the complete cooperation of the entire medical profession.

The general practitioner and the medical student who will be

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the general practitioner or specialist of the future must be enlisted. Their importance has not gone unnoticed by those intensely interested in the struggle against tuberculosis. Tuberculosis Associations, chest specialists and the College Council have gone on record advocating more intensive and extensive instruction in tuberculosis. Barrier after barrier has been met. During the war years the speeded-up and concentrated medical school curriculum left no space for enlargement. This was a convincing argument but, unfortunately, the years since the war ended have brought only a slight improvement in the situation.

Although the great increase in detailed knowledge of the various parts of the body and their respective diseases has necessitated specialization no one knows better than the specialist that the general practitioner is the foundation rock of our profession. It is he who first sees the tuberculous patient when he is only slightly ill or even asymptomatic. His awareness of the possibility of the presence of tuberculosis in his patients can only result in earlier diagnosis and earlier and more effective therapy. The general practitioner, however, is not alone in his failure to keep the disease in mind. Specialists in other fields are just as prone to overlook its presence. How many times have we seen surgical and obstetrical cases with slight coughs who are operated upon or delivered without any but the most cursory and superficial attention paid to that symptom? How many times have we seen the diagnosis made only after the patient fails to make an uneventful recovery and presents a clinical picture of low grade fever, cough and expectoration?

Re-education must be made complete in all parts of our profession. There is certainly no intention to create a vast body of experts in pulmonary tuberculosis but, rather to create an awareness of the problem, an alertness to its possible presence, and a realization of the effectiveness of early therapy. We should like to see such an educational program instituted in every medical school and we look forward to the day when every hospital with a staff of well trained chest men can extend such teaching to all the men on the staff and in the community regardless of their specialty.

As this thought in mind we approached Dean J. A. W. Hetrick of the New York Medical College. The idea of an intensive course in tuberculosis for both medical students and postgraduate students was conceived and discussed. The wholehearted reception accorded this suggestion was most encouraging and out of these meetings resulted an affiliation between the New York Medical College and the Municipal Sanatorium of the City of New York at Otisville, New York. For a beginning, the course was made an elective one

of three weeks duration for senior students during the summer months. The students were to be housed in the Staff House at the Sanatorium and teaching was to be done by the Medical Staff.

Ideally, the student should have an opportunity to observe the course of the disease over a long period of time so that its varied manifestations, its progression and healing, its treatment and emergencies might be thoroughly understood. Such a state of affairs is almost utopian in the already crowded medical school curriculum. It was our thought that an intensive course given in the atmosphere of the Sanatorium would arouse interest and dispel the unwarranted fear of the disease that exists among medical students and their practicing colleagues. By daily contact under skillful guidance a more rational approach to the disease would be instilled. The technique of isolation and the simple rules of personal protection would overcome the tuberculosis phobias so commonly encountered.

Although the course was made an elective one it was hoped that the students who took it would act as medical missionaries and would arouse enthusiasm in their fellow students. This very thing happened and the wonderful response of the students promises to make necessary several three-week courses during the summer months in order to accommodate the students applying.

The course first set up and successfully conducted in the Summer of 1947 was as follows:

### *Undergraduate Course*

#### FIRST WEEK

##### *Monday, June 23, 1947*

1 00 - 1 45 P M

Introduction to Course Orientation to Sanatorium Divisions

1 45 - 4 45 P M

Diagnosis of Tuberculosis (Case Demonstration)

##### *Tuesday, June 24, 1947*

9 00 - 12 00 Noon

Laboratory Aids and Techniques in Diagnosis Demonstration of Laboratory Methods (Tuberculin Test, Hematology in Tuberculosis)

1 30 - 4 00 P M

Roentgenology (Principles and Method) Fluoroscopy (Principles, Value and Demonstration of Technique) X-ray Classification of Tuberculosis

4 00 - 5 00 P M

Prophylaxis of Tuberculosis (Illustrated Talk)

##### *Wednesday, June 25, 1947*

9 00 - 11 00 A M

Conference on Sanatorium Admissions (Patient and Film Demonstration Case Discussion (Diagnosis and Treatment)

11 00 - 12 00 Noon

National Tuberculosis Association Classification of Extent of Tuberculosis and Clinical Status, (X-ray Demonstration)

- 1 00 - 4 30 P M  
Pathology of Tuberculosis Pathogenesis of Tuberculosis (Illustrated Talk) Demonstration of Museum Specimens Performance of Autopsy

*Thursday, June 26, 1947*

- 9 00 - 9 40 A M  
Question and Discussion Period
- 9 45 - 11 00 A M  
General Treatment of Tuberculosis (Rest, Diet, Heliotherapy, Symptomatic)
- 11 00 - 12 00 Noon  
X-ray Diagnosis in Tuberculosis (X-ray Demonstration)
- 1 00 - 5 00 P M  
Collapse Therapy in Tuberculosis Film on Artificial Pneumothorax (Indications, Contra-indications, Technique, Complications) Case Demonstration of Initial Pneumothorax Refills Film on Bronchography

*Friday, June 27, 1947*

- 9 00 - 9 40 A M  
Question and Discussion Period
- 9 40 - 12 00 Noon  
Pneumoperitoneum in Treatment of Tuberculosis Case Demonstration of Initial Pneumoperitoneum
- 1 00 - 3 00 P M  
Surgical Collapse Methods in Tuberculosis (Thoracoplasty, Pneumonolyses, Phrenic Operations, etc ) Illustrated Talk
- 3 15 - 4 45 P M  
X-ray Demonstration of Cases Before and After Surgical Procedures

*Saturday, June 28, 1947*

- 9 00 - 11 30 A M  
Operative Clinic Demonstration of Phrenic Crush and Intrapleural Pneumonolyses
- 11 30 - 12 10 P M  
Presentation of Post-Operative Cases (After Pneumonolyses, Thoracoplasty and Phrenic Operation)
- 1 15 - 4 15 P M  
Grand Clinical Conference Case Presentation and Discussion (Treatment)

SECOND WEEK

*Monday, June 30, 1947*

- 9 00 - 12 00 Noon  
Emergencies in Tuberculosis (Hemorrhage, Spontaneous Pneumothorax, Empyema, Atelectasis) Case and X-ray Demonstrations
- 1 00 - 2 00 P M  
Prognosis in Tuberculosis
- 2 00 - 4 30 P M  
Pleural Tuberculosis Tuberculosis and Diabetes

*Tuesday, July 1, 1947*

- 9 00 - 11 00 A M  
Streptomycin Therapy in Tuberculosis
- 11 00 - 12 00 Noon  
Tuberculation Therapy in Pulmonary Disease
- 1 00 - 4 45 P M  
Laryngeal Tuberculosis Case Demonstrations of Laryngeal Tuberculosis

*Wednesday July 2, 1947*

- 9 00 - 12 00 Noon  
Conference on Sanatorium Admissions (Patient and Film Demonstration) Case Discussion (Diagnosis and Treatment)

- 1 00 - 3 00 P M  
Pregnancy in Tuberculosis (Case and X-ray Demonstration)

- 3 00 - 5 00 P M  
Allergy and Immunity in Tuberculosis

*Thursday, July 3, 1947*

- 9 00 - 10 00 A M  
Differential Diagnosis (X-ray Demonstration)

- 10 00 - 12 15 P M  
Differential Diagnosis (X-ray Demonstration)

- 1 00 - 3 00 P M  
Social Aspects in Tuberculosis Rehabilitation in Tuberculosis Re-  
habilitation Case Conference

- 3 00 - 5 00 P M  
Public Health in Tuberculosis

- 6 30 - 9 30 P M  
Differential Diagnosis (X-ray Demonstration)

*Saturday, July 5, 1947*

- 9 00 - 12 00 Noon  
Tracheobronchial Tuberculosis (Illustrated Talk and Moving Pic-  
tures) Bronchosopic Clinic (Case Demonstrations)

### T H I R D W E E K

*Monday, July 7, 1947*

- 9 00 - 12 00 Noon  
Assignment of Cases to Students (History Taking and Physical  
Examination)

- 1 00 - 1 30 P M  
Ward Rounds (Discussion and Examination of Cases Worked Up  
By Students)

- 1 30 - 3 30 P M  
Gastrointestinal Tuberculosis (X-ray Demonstration)

- 3 30 - 5 00 P M  
Ward Rounds (Discussion and Examination of Cases Worked Up  
By Students)

*Tuesday, July 8, 1947*

- 9 00 - 12 00 Noon  
Ward Rounds (Discussion and Examination of Cases Worked Up  
By Students)

- 1 15 - 4 30 P M  
Differential Diagnosis

*Wednesday, July 9, 1947*

- 9 00 - 12 00 Noon  
Conference on Sanatorium Admissions (Patient and Film Demon-  
stration) Case Discussion (Diagnosis and Treatment)

- 1 00 - 3 30 P M  
Tuberculosis and Lues (Case Demonstration) Dermatology Clinic

- 3 30 - 5 00 P M  
Ward Rounds (Discussion and Examination of Cases Worked Up  
By Students)

*Thursday, July 10, 1947*

- 9 00 - 12 00 Noon  
Ward Rounds (Case Discussion and Physical Diagnosis)

- 1 00 - 3 30 P M  
Genito-urinary Tuberculosis Illustrated Talk Film on Nephrec-  
tomy Urology Clinic (Case Presentations)

- 3 30 - 5 00 P M  
Ward Rounds (Case Discussion and Physical Diagnosis)

*Friday, July 11, 1947*

- 9 00 - 12 00 Noon  
Ward Rounds (Case Discussion and Physical Diagnosis) Assign-  
ment of Cases to Students (History Taking, Physical Examination)



- 1 00 - 4 15 P M  
Ward Rounds (Discussion and Examination of Cases Worked Up  
By Students)

*Saturday, July 12, 1947*

- 9 00 - 10 45 A M  
Ward Rounds (Case Discussion and Physical Diagnosis)  
10 45 - 12 00 Noon  
Differential Diagnosis  
1 30 - 4 30 P M  
E N T Clinic Case Presentations of Laryngeal Tuberculosis and  
Ear Tuberculosis

The undergraduate course having been launched, a postgraduate course was established in order to make available to the practicing physician similar opportunities for study. The increase in tuberculosis to epidemic proportion at a time when educational facilities and medical personnel are at the lowest ebb in war-torn Europe and Asia has made this country the hope of the world. Inquiries concerning the course have been received from Europe, India, China and South America. All these pertained to the possibilities of postgraduate instruction in Diseases of the Chest. All applications were referred to the Dean of the New York Medical College within whose jurisdiction lay the acceptance of the students. As in the case of the senior students, arrangements were made to house postgraduate students at the Sanatorium Staff house. With experience gained by the first course, certain changes were made in the curriculum and the course presented was as follows:

### *Postgraduate Course*

#### FIRST WEEK

*Monday, October 20, 1947*

- 9 00 - 10 30 A M  
Epidemiology  
10 30 - 12 00 Noon  
Laboratory Aids and Techniques in Diagnosis  
1 00 - 4 00 P M  
Demonstration of Laboratory Methods (Tuberculin Testing, Hematology and Tuberculosis)  
4 00 - 5 00 P M  
Etiology of Tuberculosis (Illustrated Talk)

*Tuesday, October 21, 1947*

- 9 00 - 12 00 Noon  
1. Etiology of Tuberculosis Pathogenesis of Tuberculosis (Illustrated Talk) Demonstration of Museum Specimens  
1 00 - 4 00 P M  
2. Diagnosis of Pulmonary Diseases  
4 00 - 5 30 P M  
3. General Tuberculosis Association Classification of Tuberculosis in Relation to Pulmonary Involvement and Clinical Manifestations (X-ray Demonstration)

*Wednesday, October 22, 1947*

- 9 00 - 12 00 Noon  
Physiology of Pulmonary Diseases  
1 00 - 3 30 P M  
Diagnosis of Tuberculosis Clinical Methods (Case Demonstration)

- 3 30 - 5 00 P M  
Conference on Sanatorium Admissions

*Thursday, October 23, 1947*

- 9 00 - 9 30 A M  
Question and Discussion Period
- 9 30 - 12 00 Noon  
General Treatment of Tuberculosis (Rest, Diet, Heliotherapy, Symptomatic)
- 1 00 - 5 00 P M  
Collapse Therapy in Tuberculosis Sound Film on Artificial Pneumothorax (Indications Contra-Indications, Technique, Complications) Case Demonstration of Initial Pneumothorax Refills Sound Film on Bronchography

*Friday, October 24 1947*

- 9 00 - 9 30 A M  
Question and Discussion Period
- 9 30 - 12 00 Noon  
Pneumoperitoneum in Treatment of Tuberculosis Case Demonstration of Initial Pneumoperitoneum
- 1 00 - 3 00 P M  
Allergy in Pulmonary Disease
- 3 00 - 5 00 P M  
Pulmonary Anatomy, Pulmonary Segments and Broncho-pulmonary Disease

*Saturday, October 25, 1947*

- 9 00 - 12 00 Noon  
Operative Clinic Demonstration of Phrenic Crush and Intrapleural Pneumonolyses
- 1 15 - 4 15 P M  
Grand Clinical Conference Case Presentation and Discussion

S E C O N D W E E K

*Monday, October 27, 1947*

- 9 00 - 11 00 A M  
Emergencies in Tuberculosis (Hemoptysis, Spontaneous Pneumothorax, Empyema, Atelectasis, etc) Case and X-ray Demonstrations
- 11 00 - 12 00 Noon  
Prognosis in Tuberculosis
- 1 00 - 3 00 P M  
The Pleura in Tuberculosis
- 3 00 - 5 00 P M  
Diabetes and Tuberculosis

*Tuesday October 28, 1947*

- 9 00 - 12 00 Noon  
Laryngeal Tuberculosis Etiology, Symptomatology Clinical Course Differential Diagnosis Therapy
- 1 15 - 4 45 P M  
Laryngeal Tuberculosis Case Demonstrations

*Wednesday, October 29, 1947*

- 9 00 - 12 00 Noon  
Conference on Sanatorium Admissions (Patient and Film Demonstration) Case Discussion (Diagnosis and Treatment)
- 1 00 - 3 00 P M  
Pregnancy in Tuberculosis (Case and X-ray Demonstration)
- 3 00 - 5 00 P M  
Genito-urinary Tuberculosis Case Presentation

*Thursday, October 30, 1947*

- 9 00 - 12 00 Noon  
Differential Diagnosis in Pulmonary Diseases (X-ray Demonstration)
- 1 00 - 3 00 P M  
Social Aspects of Tuberculosis Rehabilitation in Tuberculosis Rehabilitation Case Conference
- 3 00 - 5 00 P M  
The Role of the Public Health Worker in Tuberculosis Case Finding and Follow-Up

*Friday, October 31, 1947*

- 9 00 - 10 30 A M  
Allergy and Immunity in Tuberculosis
- 10 30 - 12 00 Noon  
Cardiac Factors in Pulmonary Disease
- 1 00 - 3 00 P M  
The Surgical Approach to the Therapy of Tuberculosis (Thoracoplasty, Pneumonolyses, Phrenic Operations, etc)

*Saturday, November 1, 1947*

- 9 00 - 12 00 Noon  
Tracheobronchial Tuberculosis (Illustrated Talk and Motion Pictures) Bronchoscopic Clinic (Case Demonstrations)
- 1 15 - 4 15 P M  
Grand Clinical Conference Case Presentation and Discussion

## T H I R D   W E E K

*Monday, November 3, 1947*

- 9 00 - 12 00 Noon  
Assignment of Cases to Students (History Taking and Physical Examinations)
- 1 00 - 3 00 P M  
Gastro-Intestinal Tuberculosis (X-ray Demonstration)
- 3 00 - 5 00 P M  
Ward Rounds (Discussion and Examination of Cases Worked Up by Students)

*Tuesday, November 4, 1947*

- 9 00 - 12 00 Noon  
Antibiotic Therapy Streptomycin Therapy in Tuberculosis Technique Evaluation Aerosol Therapy in Pulmonary Diseases Experience with Promin, Penicillin and Streptomycin
- 1 00 - 3 00 P M  
Differential Diagnosis in Pulmonary Diseases

*Wednesday, November 5, 1947*

- 9 00 - 12 00 Noon  
Conference on Sanatorium Admissions (Patient and Film Demonstration) Case Discussion (Diagnosis and Treatment)
- 1 00 - 3 30 P M  
Tuberculosis and Lues (Case Demonstration) Dermatology Clinic
- 3 30 - 5 00 P M  
Ward Rounds (Discussion and Examination of Cases Worked Up by Students)

*November 6, 1947*

- 9 00 - 12 00 Noon  
Ward Rounds (Case Discussion and Physical Diagnosis)
- 1 00 - 3 00 P M  
Social Aspects of Tuberculosis Occupational, Environment, Hygiene
- 3 30 - 5 00 P M  
Fungal Diseases

*Friday, November 7, 1947*

- 9 00 - 12 00 Noon  
Ward Rounds (Case Discussion and Physical Diagnosis) Assignment of Cases to Students (History Taking, Physical Examination)
- 1 00 - 3 00 P M  
Psychosomatic Factors in Tuberculosis
- 3 00 - 5 00 P M  
Ward Rounds (Case Discussion and Physical Diagnosis)

*Saturday, November 8, 1947*

- 9 00 - 12 00 Noon  
Surgical Clinic
- 1 15 - 4 15 P M  
Grand Clinical Conference Case Presentation and Discussion

The program outlined is not inflexible and will be modified as necessary. The aim is to present not dry didactic lectures but to associate in the student's mind all the phases and aspects of the disease, physical, psychological and social as applied to the actual patient.

There is no doubt that such instruction would be best given in a general hospital where the student could observe tuberculosis along with other diseases as a long term project as part of his general clinical studies. Unfortunately, few general hospitals have adequate facilities for the care of tuberculosis and the case that is seen is discovered accidentally or is admitted as an emergency. In most cases, these hospitals become way stations or transfer points where the patient lies awaiting admittance to a tuberculosis hospital or sanatorium. Rarely are these cases treated during these often critical periods and more rarely are they utilized for teaching purposes. Until the general hospital takes a more modern and progressive view of the disease and assumes its proper place in the care and teaching of tuberculosis, we must rely upon the sanatorium and tuberculosis hospital.

The Municipal Sanatorium is ideally fitted for this purpose because of the early phases of the disease that are seen. The applicability and effectiveness of therapy can be better demonstrated to students when they are shown early or relatively early cases. Students and practitioners tend to be overwhelmed and confirmed in their belief in the hopelessness of the disease when they are confronted by far-advanced cases, large cavities and incurable chronics. To counteract this view the student should have the opportunity of observing the disease in all its phases.

Following the lectures on the various subjects listed in the schedule, the students received practical bedside training in the application of the principles of diagnosis and therapy. Experience in actual therapy was made available, specifically in the technique of collapse measures, such as pneumothorax and pneumoperitoneum. Surgical and Medical Conferences were attended where

a thorough discussion was held on the cases that had been observed and studied by the students

The entire treatment of tuberculosis loses all focus and meaning unless the patient can be returned as a useful member of society with all the psychological implications of that phrase. The Municipal Sanatorium is well aware of that factor in the treatment of tuberculosis and has set up a coordinated occupational therapy and rehabilitation program.

The students observed and were impressed with the importance of such a program. In so doing, they ceased considering the tuberculous patient as a case and began to consider each patient as an individual to be integrated into his or her environment in as normal or usual a manner as was compatible with his disease process.

The over-all picture of tuberculosis as a Public Health problem to be combatted not only locally but throughout the nation was presented to the students. Techniques of case history and follow up, principles of hygiene, and the role of hospital and Department of Health clinics were included in order that the student might understand and appreciate the machinery that has been set up to cope with the disease outside the microcosm of the hospital and sanatorium.

#### SUMMARY

It is our hope that eventually the teaching of tuberculosis will accompany the student throughout the four years of his medical school, not as an elective, but as a required course correlated with all his other subjects. In this instance, familiarity will breed not contempt but knowledge of, and respect for, a disease that thrives on ignorance.

The success of the courses given was due directly to the enthusiasm and wholehearted cooperation of the Dean and Medical Board of the New York Medical College and the Medical Staff of the Municipal Tuberculosis Sanatorium.

#### RESUMEN

Abrigamos la esperanza de que con el tiempo la enseñanza de la tuberculosis acompañará al estudiante durante sus cuatro años en la escuela de medicina, no como una materia electiva sino obligatoria y correlacionada con todas las otras materias. En este caso la familiaridad no engendrará menosprecio sino mas bien el conocimiento y respeto de una enfermedad que florece en la ignorancia.

El buen éxito de los cursos de instrucción se debió directamente al entusiasmo y activa cooperación del Decano y Junta Médica del Colegio Médico de Nueva York y el Claustro Médico del Sanatorio Municipal para Tuberculosos.

# Technique of Caulfeild's Inhibitive Test also of Tuberculo-Complement Fixation Test\* For Serological Anticipation of Tuberculous Disease (With Data Supplemental to Publication of 1925)

M FLORENCE MACLENNAN, B.A., Serologist  
Toronto, Canada

## *Preface (a)*

"The Inhibitive reaction of Caulfeild is specific for tuberculosis" (A.C.N.) We consider both the Inhibitive and Fixation reactions to be specific for this disease

The fifty page symposium "Foreseeing and Forestalling Tuberculosis\* (Twenty Years' Observations on the Approach of Tuberculous Disease)," by Ogden, Anglin, Kruger, Norwich, O'Sullivan, Macintyre, and sixteen collaborators, appeared in "Diseases of the Chest" of July-August 1946. Immediately, enquiries concerning the latest technique of the tests came from abroad as well as from America. Possibly others were already proceeding with the tests, employing the technique as given in a former symposium, "The Tuberculo-Complement-Fixation and Inhibitive Tests," by Caulfeild, A. H. W., et al, in the "American Review of Tuberculosis," XI 508, 1925. When our recent Director of Laboratories, Dr A. C. Norwich, was consulted, he advised that our Chief Serologist, Miss M. F. Maclennan, be asked to re-write the latest technique. This is presented herewith following the next several introductory paragraphs.

The use and value of these tests are given in the following excerpts from the text of the symposium.

"We know that a positive tuberculin skin test signifies that tuberculous infection has taken place. If, months or years later, symptoms appear, or x-ray films demonstrate a lesion, disease has already developed. Are there any means by which in this *blackout period* we may be informed of such serious transition from infection to disease before it actually happens? We believe that serial serological tests indicate that the infection is no longer dormant and that a transitional stage has been reached which, if unrecognized and untreated will lead to active clinical tuberculosis clearly demonstrable by routine methods" (G.C.A.)

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\*Presented at the 7th Annual Meeting of the American College of Chest Physicians, Cleveland, Ohio, May 31, 1941, by W. E. Ogden, M.D., F.C.C.P.

†Limited number of reprints available

"We have presented evidence that by means of serological tests it may be possible to diagnose tuberculosis six months to two years before the appearance of clinical signs and symptoms, and that by the addition of fractional daily amounts of rest during this pre-clinical stage, the onset of manifest disease may be prevented. As the average incubation period of tuberculosis is three to five years, it should not be hard to believe that immunological reactions occurring in the body during that time are reflected in the serum."

"Groups most easily tested and supervised are, nurses in training, and tuberculosis contacts." It would be logical to test all tuberculin positive individuals as they have been contacts. "In our hospital School for Nurses, we do not wait for an annual x-ray film to demonstrate a lesion in its early stage, when, of course, it is too late for prevention. We are anticipating clinical or x-ray evidence of disease by biological tests and precluding it by extra hygienic care." "In 20 years regular testing of over 2,500 tuberculosis contacts and nurses, only two cases have developed without previous serological warnings, and none where the prescribed extra rest has been taken." The greater part of the clinical work has been done at the Toronto Western Hospital.

Another problem-type of case which we have been solving by serology, is the one with the "spot" found incidentally by x-ray, and without symptoms. "If silent minimal tuberculous lesions found by mass x-ray survey, appear possibly healed, and if they give normal serum reactions, the patient is allowed to remain at work, pending further serology. If the tests change and indicate biological tuberculosis and therefore potential clinical disease, the individual is disqualified for work and rest is ordered, if the tests remain normal, his work is not interrupted."

W E Ogden ED, MD, FACP, FCCP

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Toronto, Canada

### *Preface (b)*

Having observed, over a number of years, the results in many thousands of tests, I am firmly convinced of their reliability and value to the painstaking and patient clinician for diagnostic and prognostic purposes in biological (pre-clinical) and in clinical pulmonary tuberculosis.

Early in the serological investigation of tuberculosis by the late Doctor A H W Caulfield, Miss Macleennan became one of his technicians and for over twenty-five years, has most conscientiously and effectively toiled in this field. "The work of

Science is to substitute facts for appearances, and demonstrations for impressions" (Ruskin) We are convinced that, above all others, she is eminently qualified to make this record

Arthur C Norwich, M.B.,  
Recent Director of Laboratories, D V A

23 Austin Crescent,  
Toronto, Canada

### *Caulfeild's Inhibitive Test — Technique*

#### *Part I Inhibitive Test*

In complement fixation tests the antigens are usually in dilutions which are not anticomplementary, and the positiveness of results is in direct ratio to the amount of complement fixed after incubation with antigen and antibody In Caulfeild's Inhibitive Test, this technique and interpretation are reversed The antigen is used in dilutions which *are* anticomplementary, and the positiveness of results is in direct ratio to the amount of complement remaining "free" after incubation with antigen and antibody It is not a "Fixation" antigen in the accepted meaning of that term

The reaction between Inhibitive Antigen and a positive serum apparently takes place before addition of complement, thus leaving the latter "free" until the haemolytic system is added This property of a positive serum, designated "Inhibitin" by Caulfeild, counteracts the anticomplementary factor in the antigen If the serum being tested does not lessen the anticomplementary strength of the antigen, complement when added will, of course, be absorbed by the antigen and haemolysis will not result after addition of the haemolytic system It would seem that such an antigen might be adapted to a precipitation test, but so far attempts to do so here have not been successful

#### *Points stressed for accuracy of results (details given later)*

1) Buffered saline must be used in order to bring all the reagents as nearly as possible to pH7 Acidity will cause irregularities and false positives

2) Sera to be tested must not remain on clot at room temperature longer than 24 hours, nor on clot in refrigerator more than 36 hours

3) Sera held over from one test to the next as controls for Inhibitive test must be tightly corked to prevent evaporation, and kept in refrigerator

4) Anti-sheep cell haemolysin must be accurately controlled, both by titration and by removal from the sera by absorption with sheep cells The latter has been found neither necessary nor desirable for the fixation test with its overnight incubation



5) Using complement only from pre-tested guinea pigs will prevent many unsatisfactory tests

6) When haemolysin and sheep cells are combined for haemolytic system, the mixing should be done quickly and just previous to use, otherwise agglutinins will interfere with the action of the complement

*Equipment required* Incubator for growing tubercle bacilli, waterbath 37.5° C and Centrifuge

*Glassware* Test tubes for blood specimens and sera 1/2" x 4"

For diluting sera Standard Kolmer Wassermann tubes

For final test 3/8" x 3" (if "micro" technique used)

*Note* Previous to 1939, the last mentioned tubes were imported from Europe. It has been found that those purchased since that date, made of American glass, were unsatisfactory for use with Inhibitive antigen (causing considerable interference with the action of the complement) until they had been repeatedly cleansed and resterilized in hot air oven at 160° C. Allowing them to remain in cleaning fluid (sulphuric acid and pot. bichromate) was not effective in removing the substance causing trouble. This interference with action of complement was noticeable only to a slight degree in the Fixation Test.

*Pipettes* For diluting and pipetting sera, preferably 0.5 cc. to tip

All glassware should be very thoroughly rinsed after cleansing to remove any trace of soap, and sterilized. Here again it should be noted that some of the newer cleansing preparations have not been satisfactory for glassware used in this test.

*Tubercle Bacilli for Antigens* (1) For Inhibitive Antigen Human tubercle bacilli growing rapidly on 5 per cent glycerine beef or veal, peptone or trypsin broth, pH 7.4 to 7.6, temperature 38 to 39° C for 5 weeks (Flat-sided, quart size flasks with about 150 cc. broth in each were found satisfactory). At end of 5 weeks flasks are placed, upright, in Arnold sterilizer for 45 to 60 minutes, allowed to cool at room temperature, contents then filtered through rather coarse filter paper, and, while tubercle bacilli are still in filter paper, rinsed once with buffered saline, then dried in incubator, 38 to 39° C by placing the filter paper containing tubercle bacilli in a wire basket. When thoroughly dry, store in glass containers in dry place.

*Note* Tubercle bacilli grown on synthetic medium have not been found suitable for Inhibitive antigen, probably due to lack of lipoids, but they are satisfactory for Fixation antigen.

*Saline Solution* 0.9 per cent NaCl in distilled water, buffered to pH 7 (or very slightly below). We have found secondary sodium phosphate  $\text{Na}_2 \text{HPO}_4$ , dibasic, and primary potassium phosphate  $\text{KH}_2\text{PO}_4$  monobasic (Clark's "Determination of Hydrogen Ions,"

Soerensen's Phosphate Mixtures, table 27, p 114) the most satisfactory Allowance is made for the buffer solution being one half isotonic

Quantity for 1 liter only

Stock solution of buffers

Pot Phos 0.908 gm in 100 cc distilled water

Sod Phos (dried for two weeks before using)  
2.375 gm in 200 cc distilled water

To 900 cc distilled water add NaCl 8.55 gm

Stock Solution Pot Phos 30 cc

Stock Solution Sod Phos 70 cc

Sterilize in autoclave or Arnold

*Guinea pigs* Only normal pigs are used and these are previously tested in lots of 12 by withdrawing about 4 cc samples of blood from the heart. Only those are used which have a sufficiently high titre of complement (1 unit not less than 1:40), contain only a negligible amount of natural anti-sheep cell haemolysin, if any, and are not sensitive to the antigens. Fresh complement should be obtained for each test, although any remaining over may be used within two or three days if kept frozen in refrigerator, diluted 1:10 with buffered saline solution.

*Preparation of sera* After clots are separated, centrifuge about 1400 R.P.M. for 20 minutes. As mentioned before, sera should not be left on clots longer than 24 hours at room temperature, nor on clots, more than 36 hours when in refrigerator.

Pipette only clear supernatant serum from each specimen into 3 tubes ( $\frac{1}{2} \times 4$ ) as follows (1) 0.45 cc (2) 0.45 cc (3) Remainder of clear serum for fixation test. Inactivate 30 minutes at 56° C. Tubes are tightly corked and kept in refrigerator as controls for next Inhibitive test. When there are intervals of only two or three days between tests, sera kept thus will be found satisfactory. The other tubes are also kept in refrigerator, plugged with cotton.

*Removal of Natural Anti-sheep cell Haemolysin* from sera used for Inhibitive test. On the morning of the test, add 2 drops of washed, packed sheep cells to each of the plugged tubes containing 0.45 cc serum, shake to mix, allow to stand at room temperature 15 to 20 minutes (preferably not longer because of tendency to become anticomplementary), centrifuge 30 minutes about 1400 R.P.M.

*Diluting sera* While titrations are being incubated, pipette 0.1 cc from each specimen of serum (0.5 cc pipette) into Standard Wassermann size tube, and add 0.9 cc saline solution with a 5 cc pipette, separate racks being used for the fixation serum dilutions, which have not had sheep cells added.

*Sheep Cells* Defibrinate with glass beads (This was found pre-

ferable to the use of sodium citrate), and wash four times with buffered saline, centrifuging 15 minutes the last time

*Inhibitive Antigen* Extract in incubator 38 to 39° C two grams dried, human tubercle bacilli (previously broken into fine granules with a pestle) with 100 cc equal quantities of absolute ethyl alcohol and ether (for anaesthesia), the latter from *copperlined* container, for 4 weeks in glass stoppered bottle Shake bottle daily during this period sufficiently to re-suspend tubercle

At the end of four weeks, pipette the extract into two 50 cc tubes (Roseneau centrifuge tubes are convenient), centrifuge at high speed for 30 minutes, then carefully decant or pipette supernatant into a porcelain evaporating dish 150 cc capacity and place in incubator 38 to 39° C until all liquid has evaporated—24 to 36 hours Re-dissolve the deposit remaining by holding the evaporating dish partly submerged in water bath at 56° C and rinsing it into a small, glass stoppered bottle with small quantities of the 50-50 alcohol-ether, using a 2 cc or 5 cc pipette (total of approximately 10 cc for this amount of extract) Use only sufficient alcohol-ether to cause the cloudy solution in bottle to just clear or become opalescent when the bottle is held in water bath at 56° C for one or two minutes One might consider it a saturated lipoidal solution Store in dark at room temperature

*Alternative, original method* After evaporation, rinse deposit into small bottle with sufficient alcohol-ether to make a 2 per cent solution Inhibitive Antigen should remain stable for a month If it becomes too anti-complementary before this time, a small quantity of alcohol-ether may be added to compensate for evaporation This extract is ready for use after standing a few days

*Dilution of Inhibitive Antigen for each day's Test* Hold the small bottle of antigen in water bath at 56° C until solution clears Using a slightly warm 0.5 or 1.0 cc pipette, measure the amount required for all the dilutions into a warm tube While slowly revolving tube, add, with a 5 cc or 10 cc pipette, sufficient buffered saline, previously heated in small flask to about 60° C, to give required dilution Mix well For the second dilution, one half strength of first, transfer part of this first dilution to another warm tube and add an equal quantity of heated saline solution and from this latter dilution make the third dilution, one-half strength of second, using the heated saline solution throughout If it is found necessary after titration to alter dilutions, commence again with the undiluted extract instead of trying to modify dilutions already made Allow antigen dilutions to cool at room temperature before using The anti-complementary dilutions required (ratio 1  $\frac{1}{2}$   $\frac{1}{4}$ ) are often found to approximate 1:40, 1:80, 1:160, but may vary considerably

*Daily titrations*

(1) Haemolysin (Supposing approximate titre to be 1 1000 equals 2 units, as previously determined by any standard method) Place 5 ( $\frac{3}{8}$ " x 3") tubes in a rack

<i>Tubes for Inh Haemolysin</i>	<i>1</i>	<i>2</i>	
Buffered Saline Solution	0.2 cc	0.2 cc	
Complement 1 20	0.1 cc	0.1 cc	
<i>For Fix'n Haemolysin</i>	<i>1</i>	<i>2</i>	<i>3</i>
Buffered Saline Solution	0.2 cc	0.2 cc	0.2 cc
Complement 1 30	0.1 cc	0.1 cc	0.1 cc

Incubate one hour in water bath at 37.5° C

Just before the end of this period, make up small amounts of haemolysin and sheep cell mixtures (Standard Kolmer Wassermann tubes are convenient size for this) as follows

<i>Tubes</i>	<i>1</i>	<i>2</i>	<i>3</i>
Haemolysin (1 1000)	0.25 cc	0.25 cc	0.25 cc
Saline Solution	0.25 cc	0.5 cc	0.75 cc
Dilutions are now	1 2000	1 3000	1 4000

Mix, and discard 0.25 cc from second and 0.5 cc from third tube. To each tube add, mixing quickly, 0.5 cc sheep cell suspension 1 20, thus obtaining three "mixtures" containing 1, 1/3 and 1/4 units, approximately, for fixation test. To the three tubes for fixation haemolysin titration, add 0.1 cc of each of these three "mixtures". To the two tubes for Inhibitive Haemolysin titration, add 0.1 cc of mixtures containing 1/3 and 1/4 units respectively.

Re-incubate 30 minutes and read. If the unit of haemolysin (1 1000, as previously determined) is correct with this particular complement, the readings will be, for Inhibitive haemolysin titration CH, ACH and for Fix'n Haemolysin titration, CH, ACH, PH. As barely two units of haemolysin are used for the Inhibitive test, the dilution required according to above example would be 1 2000. As two or more units are used in the Fix'n test, the dilution would be 1 1000. This is actually more than two units, since, in order to save time, the incubation period for Inhibitive complement titration is used for both these titrations, whereas with incubation period for the complement fixation titration less than this amount of haemolysin would be absorbed. The arbitrary complement dilutions of 1 20 for Inhibitive and 1 30 for Fixation haemolysin

titrations are chosen because they approximate those usually required in the final tests. Daily titration to determine dilutions of Inhibitive Antigen and Complement (Supposing anti-complementary dilutions of antigen are 1 40, 1 80, 1 160)

<i>Tubes, 1st row</i>	<i>1</i>	<i>2</i>	<i>3</i>
Buffered Saline Solution	0.1 cc	0.1 cc	0.1 cc
Inh Ant 1 40	0.1 cc	0.1 cc	0.1 cc
Complement	0.1 cc (1 10)	0.1 cc (1 20)	0.1 cc (1 30)

2nd row Same as above except that antigen dilution is 1 80

3rd row Same as above except that antigen dilution is 1 160

It is advisable to set up 3rd row in duplicate

Complement dilutions may be extended in one row up to 1 70, using 0.1 cc of each dilution, 0.2 cc of saline solution and omitting antigen, to determine one unit

Incubate in waterbath at 37.5° C for one hour

Add 0.1 cc haemolytic system (mixture of equal quantities sheep cells 1 20 and dilution of haemolysin equivalent to almost two units according to the preliminary titration). A small quantity should be prepared just before needed. After addition of haemolytic system, incubate ½ hour and read.

The strength of complement to be used in the final test is that which will produce just the commencement of haemolysis in the weakest dilution of antigen. For example

<i>Complement</i>	<i>1 10</i>	<i>1 20</i>	<i>1 30</i>	<i>1 40</i>	<i>1 50</i>	<i>1 60</i>	<i>1 70</i>	<i>1 80</i>
1st row (Antigen 1 40)	NH	NH	NH					
2nd row (Antigen 1 80)	PH	NH	NH					
3rd row (Antigen 1 160)	CH	PH	NH					
Saline control				CH	CH	CH	ACH	PH

If the second tube in antigen dilution 1 160 shows haemolysis which is just barely discernible, complement dilution 1 20 would be indicated, i.e. three units according to the saline control in above example. Two and a half units or more of complement should be used. Thus in the final test the weakest dilution of antigen in control tube will be almost completely anti-complementary.

*Final Inhibitive Test* (A control rack with several sera from

previous day's test, and antigen controls for each dilution, is included) Racks are shaken after addition of each reagent

*Four tubes for  
each serum*

	1	2	3	4
Serum (1 10)	0 1 cc	0 1 cc	0 1 cc	0 2 cc
Antigen	0 1 cc (1 40)	0 1 cc (1 80)	0 1 cc (1 160)	omit

Incubate in waterbath at 37.5° C for 20 minutes

Add 0.1 cc complement throughout according to strength determined by titration and re-incubate 1 hour in water bath at 37.5° C

Add 0.1 cc haemolytic system (combined just before required) and re-incubate until negative and positive controls show approximately the same degree of haemolysis as in previous test and antigen controls are NH, NH, PH

As it has sometimes been difficult (due to the variability of complement and due to the antigen becoming slightly more anti-complementary between time of titration and use in test) to determine the correct dilution of complement, it has been found very helpful to first set up one rack with 4 or 5 control sera from the previous day's test and the same number from the day's specimens, and have it precede the regular test by about half an hour. If, during the final incubation period of this "test" rack it is found that too much or too little complement had been used, the racks for the main test could then be incubated a longer or shorter period before adding haemolytic system, and also the amount of haemolysin could be changed if necessary, thus making adjustment before the final incubation period.

*Addition of Haemolytic System to Inhibitive Test* Add first to rack containing control sera and antigen controls, noting time, then add to remaining racks singly or by two's, noting time. In order to obtain uniformity of results, no definite time is stipulated for this final incubation. When the antigen controls in the first rack show NH, NH PH (?) and the repeated control sera show approximately the same degree of haemolysis as in the previous day's test, remove this control rack, and allow the remaining racks the same length of time in water bath—usually 30 to 60 minutes.

Readings are made at once and also after racks have been in refrigerator overnight.

*Strength of a new antigen* is determined simply by comparing results of a few sera with those obtained with the antigen in use.

*Interpretation of results* The average serum from a clinically nontuberculous adult will cause partial or complete haemolysis

in the tube containing the least anti-complementary dilution of antigen, but not in those containing the more anti-complementary dilutions

*Terminology used in reporting readings* (Occasionally, slight modifications have to be made if the antigen proves to be more or less anti-complementary than indicated by preliminary titration) NH is expressed by "4," PH by "3," PH plus by "2," ACH by "1," CH by "0 "

<i>Readings</i>	<i>Original Terminology</i>	<i>Later Terminology</i>
1000	First class	4 plus plus
2000-3000	2nd plus	4 plus
4000-4100	2nd class	3 plus
42+00	2nd minus	2 plus
4200	3rd plus	1 plus
4300-4420	3rd class	negative
4430-4440	Indifferent	minus

The "Indifferent" result, where the antigen has not been acted on by the serum to any appreciable extent, is noticed more frequently with sera from infants than from adults. It has been considered an unfavorable indication when occurring with sera from clinically tuberculous adults. The "Third Class" or "Negative" is the average result shown by clinically normal adults. With reference to these so called "normal" results, the following is quoted from reprint of Caulfeild's article in "The American Review of Tuberculosis," 11 6, August, 1925

"If obtained in the tuberculous with, for instance, fever and malaise, we believe the prognosis to be poor, although it has the reverse significance if the case is arrested, is without fever and is doing well "

With reference to positive results, (ie, second class or three plus) the following is quoted from the same article (this) "serological finding indicates biological activity and likely therefore in the majority of cases to be clinically evident later "

The very strongly positive results (4 plus and 4 plus plus) are obtained rather infrequently

Of 800 normal guinea pigs tested with Caulfeild's Inhibitive antigen over a period of ten years, three showed a 2 plus and one a 3 plus reaction

Positive Inhibitive reactions have been frequently observed in cases of carcinoma (diagnoses from autopsy records)

Other lipoidal extracts from tubercle have been tested as "inhib-

itive" antigens and results compared with those of Caulfeild's. Of these, an acetone extract of tubercle, and an alcohol, ether, acetone extract seemed to parallel most closely the results obtained with the alcohol-ether extract. Some antigens tested with this technique were unstable, others non-specific, as in the following examples

*Alcohol-ether* extract of tubercle bacilli previously extracted with toluol for nine days,—less stable and results positive with normal guinea pig sera

*Toluol extract* of tubercle bacilli evaporated and sediment re-suspended with alcohol-ether —results positive with normal guinea pig sera

*Alcohol-ether extract of B diphtheriae*—positive results with normal guinea pig sera, antigen itself haemolytic for sheep cells when used in dilutions required by inhibitive technique

*Alcohol-ether extract of B smegmatis*—positive results with normal guinea pig sera

A noticeable similarity in many of the results obtained with alcohol-ether extracts of tubercle, diphtheria and smegma bacilli would indicate some common factor

*Kolmer's Wassermann Antigen*—Reversed readings in antigen controls, results unlike those obtained with alcohol-ether extract of tubercle bacilli

*Cholesterin*—reversed readings in antigen controls (It may be of interest to note here that a 1/400 saline dilution of a 2 per cent suspension of cholesterin in alcohol, the percentage used in Wassermann Antigens, also resulted in reversed readings when used in place of antigen with the routine Wassermann technique, which would suggest the possibility that this reagent might be responsible for reversed readings, other than those caused by natural anti-sheep cell haemolysin, occurring in the Wassermann test)

A small quantity of *histamine* added to sera did not alter inhibitive reaction

Tests were made to determine whether more positive Inhibitive reactions occurred with sera containing an excessive amount of natural anti-sheep cell haemolysin (i.e., before absorption with sheep cells). There was found to be no parallelism

The late Dr W Ray Hodge, in an article published in the Journal of Immunology, Vol VII, No 3, May 1922, stated that the "substances responsible for the inhibitive reaction of Caulfeild are contained almost wholly in the euglobulin fraction of the serum." This conclusion was based on tests with the euglobulin fraction of sera precipitated with carbon dioxide



During the past year, total protein, globulin and albumin estimations were made in the chemical laboratory\* on a few sera sent from the chest clinic for serological tests, to determine whether "Inhibitin" might be related to an increase in any one of these fractions. Although, unfortunately, it was not possible to have many estimations made, the percentages in Table I indicate that sera showing positive Inhibitive reactions are not limited to those which are above or below the normal range in any one of these fractions. The twenty-two globulin and albumin estimations were made on the same sera, and since they all happened to be within the normal range, the percentages are the same for both.

A record was made of 283 sedimentation rates on sera (from male, chest clinic patients) on which Inhibitive tests were made at the same time. The figures given in Table II indicate a definite divergence in results between these two tests.

## Part II *Tuberculo-Complement Fixation Test*

Antigen —a modification of that described in Petroff's "Studies of Humoral Antibodies in Tuberculosis," as follows —Grind 0.5 grams dried tubercle bacilli, human type, plus an equal quantity

\*Courtesy of Wm C Arrowsmith

TABLE I  
Total proteins (Van Slyke Method)  
(Normal range 6.5 to 7.5 grams per cent)

	Normal Inhibitive Per cent	Borderline Inhibitive Per cent	Positive Inhibitive Per cent
34 sera within normal total protein range	17 (50)	8 (23.5)	9 (26.5)
9 sera above normal total protein range	3 (33.3)	0	6 (66.7)

	<i>Globulin</i> (Normal, 1.2 to 2.3 gm per cent)	<i>and</i>	<i>Albumin</i> (Normal 4.2 to 6.7 gm per cent)
	Normal Inhibitive Per cent	Borderline Inhibitive Per cent	Positive Inhibitive Per cent
22 sera all within normal range	12 (54.5)	6 (27.3)	4 (18.2)

of sterile, ground glass in mortar with a small quantity of toluol for 2 to 3 hours, add about 20 cc toluol and incubate in glass stoppered bottle, about 38° C for 5 to 6 days Replace in mortar and grind again until toluol is evaporated Combine 12½ cc glycerine with 37½ cc sterile distilled water, add small quantity to tubercle bacilli in mortar and grind 2 to 3 hours, then rinse with remaining glycerine and water into a small, pyrex flask (150 cc capacity) Simmer this emulsion under a reflux condenser for one hour, being careful not to allow it to boil Allow antigen to remain in flask overnight so that the large particles will settle out, then pipette into small bottles and store in refrigerator This antigen remains stable for a year

(A more sensitive fixation antigen is obtained from an acetone precipitate of filtrate from tubercle bacilli grown on broth 5 to 6 weeks An equal quantity of acetone is added to the filtrate, allowed to remain at room temperature two hours, centrifuged, and precipitate re-suspended in sufficient distilled water to make up the original volume of filtrate, with addition of NaCl to make isotonic By using half glycerine and half distilled water the antigen is made more stable This antigen has not been used routinely)

Filtrate from broth culture of *B. diptheriae* precipitated by above method does not cause fixation when combined with tuberculous sera, although the organism itself used as an antigen (Petroff's

TABLE II  
Sedimentation Rates

	Normal Inhibitive Per cent	Borderline Inhibitive Per cent	Positive Inhibitive Per cent
245 sera with drop or less than 15 mm in first hour	158 (64.5)	46 (18.8)	41 (16.7)
23 sera with sedimentation rate 15-30 mm in first hour	7 (30.4)	8 (34.8)	8 (34.8)
11 sera with rate 30-50 mm in first hour	2 (18)	1 (9)	8 (73)
4 sera, rate 50-100 mm in first hour	(1 Indifferent reaction, 25 per cent)	0	3 (75)

Method) gives results very similar to those obtained with tubercle bacilli

### *Titration of Complement*

<i>1st row of tubes</i>	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>	<i>5</i>	<i>6</i>
Complement	0.1 cc	0.1 cc	0.1 cc	0.1 cc	0.1 cc	0.1 cc
dilutions	(1:40)	(1:50)	(1:60)	(1:70)	(1:80)	(1:90)
Antigen	0.1 cc	0.1 cc	0.1 cc	0.1 cc	0.1 cc	0.1 cc
(usually about 1:150)						

Second row same as above, omitting antigen and using 0.2 cc buffered saline solution throughout

Place rack in refrigerator (about 8° C) for one hour, then in water bath (37½° C) for ½ hour, add 0.1 cc haemolytic system (equal quantities of 1:20 sheep cells and about 2½ units of haemolysin), incubate 30 minutes longer in water bath and take readings

As this is not a very sensitive antigen, the dilution of complement showing almost complete haemolysis in titration tube containing antigen, and complete haemolysis in the saline control tube is considered one unit, and in the final test 2, 2½ and 3 units are used. Example for test

<i>4 tubes for each specimen</i>	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>
Serum (1:10)	0.1 cc	0.1 cc	0.1 cc	0.2 cc
Antigen dilution	0.1 cc	0.1 cc	0.1 cc	omit
Complement	0.1 cc (2 units)	0.1 cc (2½ units)	0.1 cc (3 units)	0.1 cc (2 units)

Include one rack containing 0.1 and also 0.2 cc antigen controls (without serum) and several negative and positive serum controls from the previous day's test

After addition of complement, the racks are placed in refrigerator (about 8° C) overnight. Next morning, 0.1 cc haemolytic system (made up just before needed) is added throughout, to the control rack first and then to the remaining racks, one or two at a time. Each rack is timed as it is placed in the water bath at 37.5° C. Readings are made when the sera in control rack are haemolysed to approximately the same degree as in the previous day's test, and when antigen controls with 0.1 cc and 0.2 cc show CH and ACH plus, respectively. Time required is usually twenty to thirty minutes.

Racks are, of course, thoroughly shaken after addition of each reagent.

The method of reporting readings has been as follows

<i>Original Terminology</i>	<i>Later Terminology</i>
4440 (3 units of comp )	4 plus plus
4430 (2½ " " " )	4 plus
4300 (2 " " " )	3 plus
3100 (1½ " " " )	2 plus
2000 (1 " " " )	1 plus
Neg to 1000	negative

That Caulfeild considered these tests simply as an aid in diagnosis, is apparent in the following quotation from article<sup>1</sup> previously mentioned "Serological tests afford no clinical diagnosis but suggestions which should be eliminated or confirmed by other clinical methods"

These tests were first carried out under the supervision of Doctors A W H Caulfeild,\* and W Ray Hodge,\* of the Research Division of the Connaught Antitoxin Laboratories, and later under the supervision of Dr A C Norwich, as Director of Laboratories, Christie Street Hospital, Department of Veterans Affairs Assistant serologists at various times were Mina Macmillan, Florence La-Rush,\* Merle Bassingthwaight, and Dorothy Kitchen

\*Deceased

#### REFERENCE

- 1 Caulfeild, A H W, et al "The Tuberculo-Complement-Fixation and Inhibitive Tests' *Am Rev Tuberc*, 11 6, (August) 1925

# Laryngo-Tracheo-Bronchial Anesthesia for Bronchoscopy and Bronchography with Pontocaine

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Review of the literature shows a considerable variety of techniques in laryngo-tracheo-bronchial anesthesia for the procedures of bronchoscopy and bronchography. The variation is noticed in both the procedures themselves as well as in the type and quantity of the topical anesthetic. The adjuvant medication also shows a considerable difference in the types of the drugs used. The most common surface anesthetics appear to be cocaine and pontocaine. Others in use are nupercaine (Rudman<sup>17</sup>), larocaine (Benedict<sup>1</sup>), butyn (Sante<sup>18</sup>), and methycaine (Rudman<sup>17</sup>). Larocaine appeared to be a promising drug which the author and others (Jackson and Jackson,<sup>12</sup> Moorhead,<sup>14</sup> and Benedict<sup>1</sup>) have used with good results. Unfortunately the manufacturer (Hoffman La Roche) no longer produces this drug. In a survey conducted by Moorhead<sup>14</sup> it was noted that 50 per cent of his correspondents used cocaine as an anesthetic. Different authors have employed these drugs alone or in combination with each other. The quantities used vary tremendously and at times it was difficult to determine the actual amount administered as the article merely gave the percentage of the solution without specifying the total amount. In many instances an undeterminable amount was used in sprays, swabs, or tampons, making a quantitative appraisal impossible. For these reasons comparative tabulation of the amounts of the drugs introduced by the various authors could not be made in all cases. Even the articles tabulated had to have provision made for the unmeasured loss in swabs, etc.

In this study it was decided to employ pontocaine since it was felt that more and more use was being made of this drug, and that it was considered more free from the toxic reactions which occurred with cocaine (Benedict<sup>1</sup> and McReynolds<sup>13</sup>).

With respect to the adjuvant drugs, each author appears to have his own favorite. This is an understandable situation since long-continued use of any one particular drug soon makes one

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familiar with its potency in various patients as well as with its idiosyncrasies. The drugs commonly used were morphine, either alone or in combination with atropine, dilaudid, scopolamine, codeine, nembutal, sodium pentobarbital, and demerol. It was not surprising to find that the barbiturates were almost universally used in conjunction with pontocaine because of their neutralizing action in preventing the toxic symptoms occasionally seen after the administration of pontocaine. Adrenalin hydrochloride (1/1000) was also employed by most authors in various amounts added to the pontocaine solution to reduce too rapid absorption of the anesthetic agent.

Pontocaine as presently used is not in itself free from its measure of toxicity (Criciani and Nogeura,<sup>5</sup> Thomas and Fenton<sup>22</sup>) and its quota of deaths (Derbes and Engelhardt,<sup>7</sup> Richards,<sup>16</sup> Schindler,<sup>19</sup> Schoen,<sup>20</sup> Hansen and Stealy<sup>8</sup>). Reported and unreported cases of sudden death have been fairly well attributed to the drug alone. Critical reviews of the deaths indicate that in almost all cases excessive quantities of the drug have been given. The advent of the barbiturates supposedly controlled the toxic reactions, however, deaths were still observed in spite of the apparent safety which the barbiturates conferred. If the recommendations of the manufacturer on the maximum safe dosage of the pontocaine to be used for the procedures of bronchoscopy and bronchography is correct, it would appear that practically all workers who stipulate the quantity of pontocaine are employing excessive and unsafe dosages.

Tuohy<sup>24</sup> stressed that the important point to remember in the use of local anesthetics is that they must be used in small amounts. There was no question that the main difficulty in the successful use of pontocaine was one of quantity. The barbiturates though helping considerably were not the entire answer in preventing deaths. The manufacturer, in the pamphlet that accompanies the stock bottle, plainly stipulates that the maximum *safe* dose for intra-tracheal instillation should not exceed one cubic centimeter (1 cc) of the 2 per cent solution or its diluted equivalent. The total for this safe dose is twenty milligrams (20.00 mgms). Another admonition which the pamphlet stresses is that the patient, to prevent entrance of the drug into the lungs, should not inhale too deeply. Any bronchoscopist or bronchographer can readily see the impossibility of attempting to follow these tenets and yet be able to perform either one of these procedures properly under local anesthesia. The amount of the solution recommended was in most cases definitely too small for proper manipulation with spray and cannula, and no patient could be kept from unconsciously taking deep breaths while being anesthetized. As

a matter of fact in most cases the patient is encouraged to take deep breaths to spread the solution throughout the tracheo-bronchial tree. A self-consciousness on solution strengths was apparently present in the minds of almost all users of pontocaine since their articles revealed the use of several percentages of the solution below 2 per cent in order to increase the bulk of the solution for proper manipulation.

Review of the literature confirmed the anomalies between the recommendations of the manufacturer and the practical use of the solution. It was discovered that almost no worker was able to employ the recommended dose, but always exceeded it. The amounts actually used (See Table I) varied from two and one half cubic centimeters (2.5 cc) (Titcher<sup>23</sup>) for bronchoscopy to fifteen cubic centimeters (15 cc) (Poppe<sup>15</sup>) of the 2 per cent solution for bronchography. Many authors, especially bronchoscopists, could not be included in the tabulation because their articles were too vague on the actual amount of the solution used, merely mentioning the percentage of solution.

In view of the above concepts and impracticalities, and on the basis that the manufacturer probably had ample experimental work upon which to base the maximum safe dosage, it was decided to study the generally used strengths in the hope of finding an

TABLE I  
Review of the Literature on Quantities of Pontocaine Used for  
Bronchoscopy and Bronchography

Procedure	Mgms	P O N T O C A I N E		Author
		Equivalent of 2 Per cent Sol. in cc	Working Dilutions Per cent	
Bronchoscopy	50	2.5	2-0.5	Titcher <sup>23</sup>
Bronchoscopy	50*	2.5*	2-0.5	Heublein <sup>10</sup>
Bronchography	20*	1*	1	Sommerfield <sup>21</sup>
Bronchography	40*	2*	2	Boyer <sup>3</sup>
Bronchography	50-100	2.5-5	2, 0.25, 0.15, 1/1000	Castellanos <sup>4</sup>
Bronchography	60	3	2	Harwood <sup>9</sup>
Bronchography	65	3.25	0.5	Hughes <sup>11</sup>
Bronchography	120, 140, 160*	6, 7, 8*	2	Dell <sup>6</sup>
Bronchography	300	15	1	Poppe <sup>15</sup>

\*Indicates undetermined amounts used in addition to the above quantities in sprays, swabs, or tampons

effective low strength with sufficient volume for properly anesthetizing the tracheo-bronchial tree. It was felt that pontocaine was potent enough in low dilutions to be used for these purposes. The lowest uniform strength that would be effective could not be learned from the literature since most authors employed a combination of strengths beginning with the 2 per cent solution and decreasing the strength down to 1 and 0.5 per cent or even lower. The higher strengths were usually employed in the preliminary anesthetization of the mouth and pharynx, apparently on the theory that these structures are more tolerant to the stronger solution (Schindler<sup>19</sup>) than the larynx, trachea, and bronchi. One article (Castellanos, Pereiras, and Montero<sup>4</sup>) mention the use of two to four cubic centimeters (2-4 cc) of the 2 per cent solution for the mouth and pharynx and 0.25 per cent or even 0.15 per cent solution for the trachea and bronchi. On occasions these same authors have used a 1/1000 solution.

It was at once apparent when the literature was studied that the problem with respect to the solution was one of sufficient bulk to permit instillation and spread into the tracheo-bronchial tree. At the same time this solution had to be of such strength that it would be nontoxic, but still give an effective, sustained anesthesia to permit a leisurely performed bronchoscopy or bronchography, and yet meet the manufacturer's limitation of total dosage. No such one-strength solution was being used in the literature. Trial and error evolved a solution of 0.25 per cent strength which was found effective for surface anesthesia in bronchoscopy and bronchography. This solution was made by placing one cubic centimeter (1 cc) of 2 per cent pontocaine into a ten cubic centimeter (10 cc) glass cylinder, adding eight minims of adrenalin hydrochloride (1/1000) and diluting to eight cubic centimeters (8 cc) with sterile physiological salt solution. This solution was considered ideal inasmuch as it had already been tested for sufficient surface anesthesia and had what appeared to be the proper bulk to manipulate. It also had the vasoconstrictor action which most workers desired because of the adrenalin content.

Having standardized the one-strength solution, it was decided to standardize the adjuvant medication for purposes of control. Morphine in combination with atropine in full doses was used simply because the author was more familiar with its action than other drugs and probably the same could be said with other authors since most of them use this combination. No barbiturates were added in this study. It was noticed with this combination and with the use of the 0.25 per cent solution that excellent patient control and surface anesthesia were obtained. However,



it was also noticed that more than eight cubic centimeters (8 cc ), which was the total volume that could not be exceeded, was administered thus defeating the theoretical intended use of only twenty milligrams of pontocaine (1 cc of the 2 per cent or 8 cc of the 0.25 per cent solution) It was also noted that the standard atomizer as well as the laryngeal mirror and cannula technique left much to be desired when a critical study of their use was made For quantitative conservation of solution this procedure interposed many difficulties and uncertainties which resulted in a waste of about 50 to 60 per cent of the solution most of which was swallowed or expectorated The ordinary methods of laryngo-tracheo-bronchial anesthesia have not been improved upon for many years and it was felt that something could be done to effect "economy of solution" by a better armamentarium

One improvement, of course, was the elimination of the third hand about the mouth orifice In the usual method the operator first holds the atomizer in both hands (some are skilled enough to use the standard atomizer as a "one-hand" type) while the patient or an assistant retracts the tongue for the spraying procedure It was felt that the use of a "one-hand" atomizer could dispense with the third hand at this stage A handle was accord-

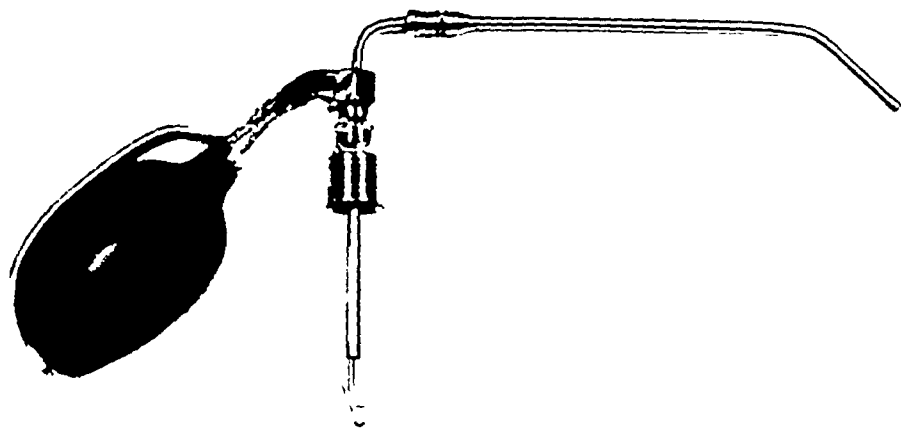


FIGURE 1 This micro-atomizer was developed from the stock Clerf atomizer in frequent use by bronchoscopists The original cannula was shortened and given the oro-pharyngeal curve The atomizer was made with a handle to make it of the "one hand" type with a double valve in its bulb which gives better, sustained compression as well as easier hand pressure than the one valve type The reservoir is of boilable glass with a capacity of about eight cubic centimeters (8 cc ) and is the same as that used on the Clerf atomizer so that the residual anesthetic can be transferred to the Clerf atomizer by simply exchanging reservoirs

ingly fitted to a standard No 15 De Vibiss atomizer and this arrangement found fairly satisfactory except that the standard atomizer had too coarse a spray and too capacious a reservoir to properly effect "economy of solution" A special atomizer was then designed by the author which met the specifications of a small reservoir and a fine spray (Fig 1)

The next step studied was the use of the separate laryngeal mirror and cannula Here the greatest waste was noted In spite of the fact that this method had been used by the author for many years, its short-comings were not noticed until the present critical study The operator had no choice but to have either the patient or an assistant hold the tongue When the patient held the tongue, its dorsum would eventually be humped up and almost completely block the line of vision The operator had to work more or less blindly, most of the time instilling the solution with the hope that it would drop upon the cords and into the trachea Even with the most cooperative of patients, it was noticed that a full view of the cords was only rarely had A goodly portion of the solution trickled down the pyriform sinuses and was swallowed When an assistant held the tongue, usually too much traction was made, resulting in pain or excessive salivation and gagging If too little traction was made, there was humping of the dorsum again with poor visibility of the cords It is true that some operators are skilled in effectively using this procedure, but when critical quantities of solution are being considered, it was felt that a more accurate localization of the structures involved as well as the direction of flow of the anesthetic were needed so that only those structures intended were anesthetized and the solution not wasted into the esophagus

To facilitate this second step a simple mirror-cannula was devised<sup>3a</sup> which permits the operator to hold the tongue himself and to make the necessary traction coordinate with the instillation of the solution Complete visibility of the posterior portion of the epiglottis as well as of the vocal cords is had at all times with this cannula Solutions can be accurately instilled only where intended without wastage

*Techniques for Bronchoscopy and Bronchography, Using the  
Micro-atomizer and Mirror-cannula*

1) Basic "one-strength" solution (0.25 per cent Pontocaine)  
This solution is simply made by adding one cubic centimeter (1 cc) of 2 per cent stock solution of pontocaine to a ten cubic centimeter (10 cc) glass cylinder Eight minims of adrenalin hydrochloride (1/1000) are then added and the solution brought

up to a total volume of eight cubic centimeters with sterile physiological salt solution

2) *Bronchography* The basic solution alone without the adjuvant medication is used for this procedure. The mirror cannula is used only for anesthetization and not for the introduction of the catheter. Spraying of the mouth and pharynx is done at ten minute intervals using the solution in the micro-atomizer sparingly. In about 20 to 30 minutes it is possible to instill several cubic centimeters of the basic solution upon the cords and into the trachea with the mirror-cannula. This is followed by the introduction of a rubber catheter (No 14 or 16 F) on a Thompson wire introducer. Occasionally it may be necessary to introduce more of the solution through the rubber catheter if too strong a cough reflex is caused by the catheter. With this technique it is possible to obtain good bronchograms with eight cubic centimeters and frequently less of the solution.

3) *Bronchoscopy* The patient is given the morphine and atropine in full physiological dose. The dosage may be increased or decreased "secundum artem" depending upon the type and size of the patient. Thirty minutes later the mouth and pharynx are sprayed with the micro-atomizer which contains about three cubic centimeters (3 cc) of the basic solution. Care is taken to fully retract the tongue and to have the patient inhale with each spraying. It was not found necessary to spray too heavily for effective anesthesia. Two or three squeezes of the bulb usually suffice. Ten minutes later a second spraying is done which is repeated again in ten minutes. In about five minutes it will be discovered that the patient experiences the sensation of numbness and inability to swallow which indicates proper anesthesia. At this point he is placed on an ear, nose, and throat chair, the tongue retracted, and one cubic centimeter (1 cc) of the solution instilled upon the vocal cords and into the trachea. The solution which is used for this procedure is the balance of the original eight cubic centimeters (8 cc) that had been prepared. It is placed in a medicine glass and taken up into the syringe attached to the mirror-cannula in one cubic centimeter or more portions as needed. It will be noticed that as soon as the solution strikes the tracheal mucosa a cough is elicited. The introduction of the solution is made gently and deliberately, drop by drop. Following the instillation the patient is asked to cough with his mouth closed. This permits the solution to be spread evenly throughout the tracheo-bronchial tree. Five minutes later a second instillation of about one cubic centimeter (1 cc) is made in the same manner. At this time the cough is considerably obtunded with a marked change in its timbre and indicates that the patient is

ready for bronchoscopy. If the cough is still high-pitched, a third instillation may be indicated. The procedure must not be hurried, nor too great quantities of solution instilled. One must refrain from "pouring in" the solution as the quantities recommended will be found of sufficient strength for proper surface anesthesia. The patient is then placed on the bronchoscopic table and given the sermon on relaxation as advocated by Jackson and Jackson<sup>12</sup>. This, as well as a darkened room, quiet, and a sympathetic attitude are of the utmost importance in successful bronchoscopy. The author makes it a rule to describe the procedure to the patient, but only when he is on the table.

Prior to introducing the bronchoscope the remaining solution in the medicine glass is transferred to the reservoir of the micro-atomizer which may still have some of the solution which was used for spraying. This reservoir is then attached to the Clerf atomizer for endo-bronchial spraying. It will be noted that the reservoirs of the micro-atomizer are the same as those used in the Clerf atomizer and therefore interchangeable. The bronchoscope is introduced in the usual manner and when it reaches the carina, the right and left main stem bronchi are anesthetized by spraying very sparingly with the Clerf atomizer which now contains the residuum of the original basic solution. On occasions it will be found that spraying of the bronchi will not be necessary. After several minutes of waiting, it will be possible to proceed with the bronchoscopy satisfactorily. Occasionally a patient is encountered who will cough when the bronchoscope is introduced far down distending the lumen with its bulk. When this contingency occurs the bronchoscope is slightly withdrawn relieving the pressure and the area gently sprayed with the Clerf atomizer. This procedure apparently satisfactorily controls the cough reflex.

Following the completion of the bronchoscopy the residual anesthetic that is left in the Clerf atomizer is placed in the ten cubic centimeter glass cylinder and the total quantity used for the entire procedure of oro-pharyngo-laryngo-tracheo-bronchial anesthesia determined by subtracting what is left from the original volume of eight cubic centimeters (8 cc). It is advocated that this be done in every case and recorded as it enables the operator to become "solution conscious" and makes him strive to conserve at all stages.

In the series of bronchoscopies reported oxygen insufflation through the side arm of the bronchoscope was used at the rate of six liters per minute as it was felt that the entire procedure was facilitated and relieved the patient of the sense of suffocation which is frequently noticed during bronchoscopy without oxygen.

4) *Simultaneous Bronchoscopy and Bronchography* The author has been recently performing both bronchoscopy and bronchography at the same sitting with the same amount of anesthesia as is used for bronchoscopy. The technique will be reported in a later communication, but is mentioned here inasmuch as it has been used in many of the patients reported in this series and since it further shows that pontocaine even in dilute solution is capable of prolonged and sustained surface anesthesia.

*Results* A total of 167 consecutive, unselected, bronchoscopies in adults were performed with the technique and innovations of instruments mentioned above. With the exception of eight cases all were ambulant patients. The eight were hospitalized for other reasons than their pulmonary manifestations. The series was considerably varied and included the following types of patients: Broncho-sinusitides, asthmatics, compensated cardiac diseases, hypertensives, stabilized coronary disease, lung abscesses, bronchiectases, pulmonary neoplasms, Hodgkin's disease, empyemata, atelectases, broncho-pulmonary suppurations, pulmonary tuberculosis, bronchial ulcerations, bronchostenoses, advanced age, and one case of severe cervico-dorsal kypho-scoliosis associated with bronchiectasis. It will be seen from the above list that the series gave the opportunity to study the technique in the usual collection of cases that may come to bronchoscopy. Many cases proved to have negative findings in spite of the fact that they presented pulmonary symptomatology of what could have been either endobronchial or endotracheal lesions, so, it may be said, that the procedure was also used in "normal" cases.

The oldest patient was 70 and the youngest 19 years of age. The average age was 39.3 years and the average weight 138.3 pounds.

To judge the adequacy of the anesthesia from the point of view of the patient, notes were kept on the cooperation of the patient as well as of the amount of coughing during the procedure of bronchoscopy. With the exception of eight (8) cases, the patients behaved well, coughed very little, and the bronchoscopy was carried out leisurely and deliberately. In these eight cases, however, there was considerable cough which necessitated additional surface anesthesia. They are discussed below. A "head-holder" was not used in any case and the entire procedure was carried out by the operator with one instrument nurse. All were strictly ambulant except the cases previously mentioned who were already in the hospital for other reasons. No ambulant case required hospitalization after bronchoscopy for any reason whatsoever.

Excessive secretions in the oropharynx were noted in only four of the patients. These required aspiration before bronchoscopy could be performed. One case salivated so profusely that the secre-

TABLE II  
Drug Dosage in 167 Consecutive Bronchoscopies in Adults

Cases	P O N T O C A I N E				
	Mgms	Equivalent of 2 Per cent Sol in cc	Working Solution cc of 0.25 Per cent	Morph Sulf Mgms	Atrop Sulf Mgms
1	40 00	2 000	16 00	22 50	0 60
1	40 00	2 000	16 00	7 50	0.20
2	30 00	1 500	12 00	15 00	0 40
2	30 00	1 500	12 00	7 50	0 20
2	25 00	1.250	10 00	15 00	0 40
3	20 00	1 000	8 00	22 50	0 60
61	20 00	1 000	8 00	15 00	0 40
8	20 00	1 000	8 00	7 50	0 20
2	18 75	0 937	7 50	15 00	0 40
8	17 50	0 875	7 00	15 00	0 40
1	17 00	0 850	6 80	15 00	0 40
1	17 00	0 850	6 80	11 25	0 30
38	15 00	0 750	6 00	15 00	0 40
1	15 00	0 750	6 00	11.25	0.30
1	15 00	0 750	6 00	7 50	0 20
1	14 50	0 725	5 80	15 00	0 40
10	12 50	0 625	5 00	15 00	0 40
1	12 50	0 625	5 00	22 50	0 60
2	12 50	0 625	5 00	11 25	0 30
1	12 50	0 625	5 00	7 50	0 20
1	12 00	0 600	4 80	15 00	0 40
2	11 87	0 594	4 75	15 00	0 40
3	11 25	0 563	4 50	15 00	0 40
2	11 25	0 563	4 50	11.25	0 30
1	11 00	0 550	4 40	15 00	0 40
1	10 05	0 525	4 20	15 00	0 40
3	10 00	0 500	4 00	15 00	0 40
1	10 00	0 500	4 00	11 25	0 30
1	9 37	0 468	3 75	11.25	0.30
1	8 75	0 438	3 50	15 00	0 40
1	8 75	0 438	3 50	11 25	0 30
1	7 50	0 375	3 00	11.25	0 30
1	6.25	0 312	2 50	11.25	0.30
1	5 00	0 250	2 00	11 25	0 30
Tot 167	2890 66	144 508	1156 05	2400 00	64 00
Average	17 37	0 865	6 92	14 43	0.383
"Normal"	20 00	1 000	8 00	15 00	0 400

tions ran into the lung alongside the bronchoscope and required continuous aspiration

Table II gives the actual dosage of the pontocaine in milligrams and equivalents in cubic centimeters of a 2 per cent solution as well as of the 0.25 per cent solution which was actually used. The comparison with the 2 per cent solution is made because a better concept is had of the small amounts of pontocaine used. The table also gives the milligrams of morphine and atropine. It will be noted that only eight (8) cases required dosages higher than those recommended by the manufacturer, but still less than any reported in the literature for bronchoscopy. Three of these cases had only 7.50 milligrams of morphine and it is felt that the total quantity of pontocaine could have been reduced had full doses of morphine been employed. One case was a chronic alcoholic of such physical mien that the full dose of 40.00 mgms of pontocaine and 22.5 mgms of morphine were entirely needed. He was the most difficult of the series. One with pulmonary abscess had the entire tracheo-bronchial tree coated with a tenacious, muco-purulent secretion which prevented the anesthetic from reaching the mucosa. It was noted throughout the series that cases of pulmonary abscess and advanced bronchiectasis were difficult to anesthetize for the same reason. Three cases were not exceptional in any manner and the excess dosage could not be based on any particular reason except that they were done early in the series before the technique was well mastered. These eight cases of "over-dosage" are analyzed in Table III.

The actual chronological protocol of cases roughly parallels the decrease in dosage shown in the table. The gradual decrease was

TABLE III  
Analysis of Cases of "Over-Dosage" (8 Cases)

Age	Weight lbs	Sex	Pontocaine Mgms	Morph Sulf Mgms	Atrop Sulf Mgms	Remarks
46	171	M	40	22.5	0.6	Chronic alcoholic
65	165	F	40	7.5	0.2	Carc LUL with bronchostenosis, severe
46	121	F	30	15.0	0.4	Normal findings
54	136	F	30	15.0	0.4	Abscess RML
48	155	F	30	7.5	0.2	Normal findings
38	129	M	30	7.5	0.2	Abscess LUL
34	180	M	25	15.00	0.4	Normal findings
29	180	M	25	15.0	0.4	Normal findings

possible as the operator became more skilled with the technique. It will be noted that several large groups (61 and 38 cases) had uniform doses. This standardization occurred when the author thought he had reached two minimum levels below which he could not go without losing the effect of the anesthetic. Subsequent cases proved, however, that a personal variable was present with each patient and that each one had his own level of susceptibility to the action of pontocaine. The operator soon got the "feel" of the anesthetic action and instilled only sufficient quantities. It will be further noted that 72 cases were done with the equivalent of one cubic centimeter (1 cc) of the 2 per cent solution (20.00 mgms) and that 87 cases with the equivalent of less than one cubic centimeter of the 2 per cent solution (less than 20.00 mgms).

The average dose for the entire series was the equivalent of 0.865 cc of the 2 per cent solution or 17.37 milligrams of pontocaine. The average dose of morphine was 14.43 milligrams and that of the atropine 0.383 milligrams. All these dosages are well within the safe limits of posological tables and, with respect to the pontocaine, below the maximum recommended dose of the manufacturer.

*Complications and Sequelae* In spite of the fact that no barbiturates were used in any case of the series, no case presented any symptomatology which could be construed as a reaction to pontocaine. The eight cases of "over-dosage" were watched closely and showed no immediate or delayed ill-effects from this drug. In the series were included six cases of severe asthma who had been personally seen in asthmatic crises on various occasions leaving no doubt as to the diagnosis with respect to their allergy. These patients were also closely watched for any toxic manifestations or precipitation of asthmatic crises inasmuch as reactions to this drug in asthmatics have occurred with sufficient frequency that Jackson and Reynolds as quoted by Benedict<sup>2</sup> have stated that pontocaine is contra-indicated in asthmatics. Criciani and Nogeura<sup>5</sup> have reported the production of asthmatic crises by the intratracheal instillation of pontocaine. The results in the six cases constitutes too small a series to draw any definite conclusions when compared with the more complete studies by the authors just mentioned, and the absence of complications in these asthmatics might have been purely a fortunate coincidence.

## SUMMARY

1) Review of the literature shows that all authors committing themselves on the actual quantity of pontocaine used for bronchoscopy or bronchography are using far more of the drug than



is recommended by the manufacturer In one case as much as fifteen times the recommended dose was used for bronchography

2) Unnecessarily large amounts of pontocaine are used for these procedures because of the inadequacies inherent in present techniques and instrumentarium

3) A "one-hand" micro-atomizer and mirror-cannula which permit use of small doses of pontocaine are described

4) A technique which makes possible bronchoscopy and bronchography with the use of 20 00 mgms (1 cc of 2 per cent solution) or less of pontocaine as a 0 25 per cent solution with only morphine and atropine in full doses as adjuvent sedation is described

5) An unselected, consecutive, series of 167 bronchoscopies in adults performed with these techniques using an average of 17 37 mgms of pontocaine (0 865 cc of 2 per cent solution) with no complications attributable to pontocaine is reported

6) This entire series was performed without the use of any barbiturate to counteract the reactions to pontocaine

7) Pontocaine in 0 25 per cent solution is a safe, effective, and long-lasting surface anesthetic suitable for the procedures of bronchoscopy and bronchography

## RESUMEN

1) La revista de la literatura revela que todos los autores que se han declarado acerca de la verdadera cantidad de pontocaína que usan para la broncoscopia o la broncografía están usando una cantidad de la droga mucho más grande de la que recomienda el fabricante En un caso se usó para la broncografía una cantidad quince veces más grande que la dosis recomendada

2) Se emplean cantidades supérfluas de pontocaína en estos procedimientos debido a las imperfecciones inherentes a las técnicas e instrumentos que se usan actualmente

3) Se describe un micro-pulverizador y espejo-cánula usados con una sola mano, que permiten el empleo de dosis pequeñas de pontocaína

4) Se describe una técnica que permite la ejecución de la broncoscopia y la broncografía, con 20 00 mg (1 cc de una solución al 2 por ciento), o menos, de pontocaína en una solución al 0 25 por ciento, con dosis completas de morfina y atropina como sedantes auxiliares

5) Se informa sobre una serie consecutiva, no seleccionada, de 167 broncoscopias en adultos llevadas a cabo mediante estas técnicas, usando un promedio de 17 37 mg de pontocaína (0 865 cc de una solución al 2 por ciento), sin ninguna complicación imputable a la pontocaína

6) Se llevo a cabo esta entera serie sin usar ningun barbiturato para neutralizar las reacciones a la pontocaina

7) La pontocaina en solucion al 0.25 por ciento es un anestésico de superficie salvo, eficaz y de accion prolongada, adaptable a los procedimientos de la broncoscopia y la broncografia

All the instruments mentioned in this paper including the mirror-cannula and the micro-atomizer are available from the George P. Pilling & Sons Company, 3451 Walnut Street, Philadelphia, Pennsylvania, to whom the author has given the specifications for the manufacture of both these instruments

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# Intratracheal Atomization in the Treatment of Infectious Diseases of the Respiratory System

## Preliminary Report

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The treatment of infectious diseases of the respiratory tract with aerosols has become quite popular during the last few years, due in particular to the use of antibiotics. At present, nebulizers are used for this procedure in which the thick particles are condensed in the apparatus allowing only the outflow of very fine and small particles, less than two micra in diameter.

The common sprayers cause an outflow of droplets much thicker and we have demonstrated in our works on Mucosography of the Respiratory System (Radiology, July 1942) that these droplets reach by gravity and pulmonary aspiration the terminal bronchi and the pulmonary alveoli.

Harold A. Abramson of the Staff of the Commanding General Technical Division, Chemical Warfare Service, in his work on Aerosol Therapy of the Lung and Bronchi with Special reference to Penicillin and Hydrogen Peroxide (New England Medical Center, VIII, 1946), recommends the use of our technique of atomization in the general treatment of the diseases of the respiratory system where great amounts of liquids should be used.

We began our studies in the Department of Tuberculosis of the Faculty of Medicine of the University of Havana (Instituto de Vías Respiratorias, Servicio del Profesor Doctor A. Antonetti). We selected a group of patients who presented different pulmonary suppurations such as bronchiectasis, abscess of the lungs, gangrene of the lungs, etc. The first part of our investigation was directed to prove under what conditions could this method be applied. The anesthesia to be used was considered, the volume and concentration of the solution used, and its tolerance by the bronchial tract.

Tests were performed with penicillin, streptomycin, hydrogen peroxide and sulfa drugs. Finally we decided to use penicillin in the first series of applications, bearing in mind its antibiotic action and its known tolerance.

Direct examination was made of the patients' sputum from the

bacteriological point of view Cultures were carried out routinely in all the cases Several determinations in series were performed to demonstrate the levels or concentrations of the antibiotics in the blood Other determinations were made for the purpose of studying the conditions of absorption, retention or elimination of antibiotics in the sputum Comparative studies with other methods of therapy by inhalation were made

### *Technique*

The technique of intratracheal atomization is not a difficult one We take a long sprayer that gives a very fine atomization, the end may be placed easily in the larynx, behind the epiglottis (Fig 1) or in the trachea under the vocal cords The apparatus we designed is very satisfactory and we are pleased with the results obtained

We start our procedure by anesthetizing the pharynx, larynx and the trachea by spraying a solution of  $\frac{1}{2}$  per cent pantocaine During the atomization of the pantocaine we have the patient lean towards the side we are going to treat and we have him inhale strongly in order to anesthetize the trachea and the bron-

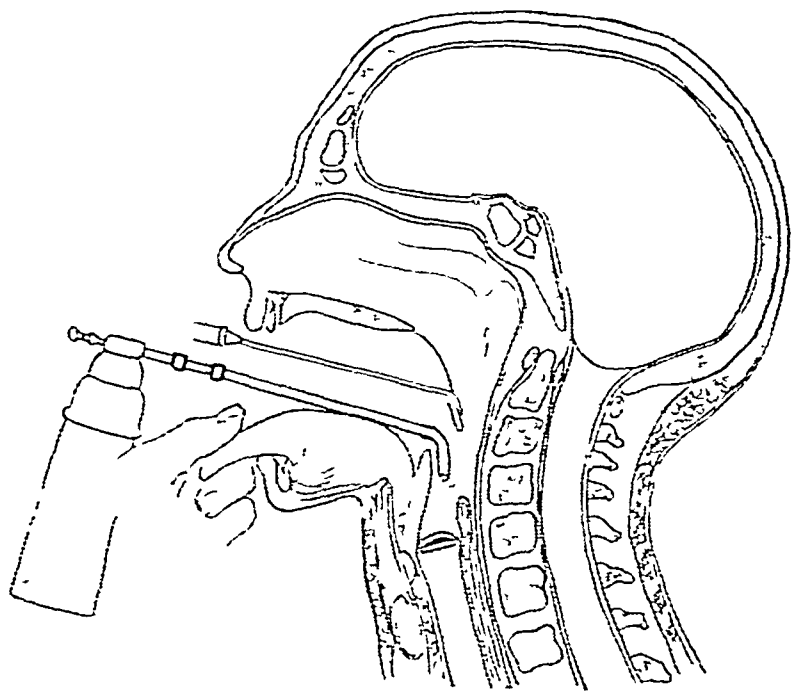


FIGURE 1 The atomizer in the larynx above the vocal cords

chial tract on that side. After waiting a few minutes so that the anesthesia is well established, we place our sprayer in the trachea and then commence to spray with the solution we have adopted for this technique. Before the sprayer is placed in the trachea, its container is connected to a rubber tube with an air compressor allowing a pressure of six or seven pounds. The patient must be seated in a straight position with the head straight up and the body completely bent towards the side we are going to treat, and bent to the front or to the back according to the pulmonary segment which is the object of the treatment. Right after the atomization the patient is placed in a special position corresponding to the pulmonary segments where the lesion is located and must remain in this position as long as possible trying not to cough. Trendelenburg's position should be always used for the upper lobe. The quantity of the spray solution varies according to the kind of diseases and the substance used, 20 cc of an aqueous solution may be sprayed in one or two minutes.

### *Laboratory Investigations*

For the exact bacteriological control of the sputum we have used 5 per cent blood-agar as culture medium. The determination of the antibiotic action was done following the technique of the Oxford investigators. In Petri dishes with solid agar medium, we add staphylococcus aureus (strains received from Washington) culture diluted to 1/10. After keeping it 24 hours in refrigerator, it is placed on the surface of the agar. The rings are filled with the blood, sputum or other secretions to be tested for antibiotic properties. The Petri dishes are refrigerated for 24 hours, after this period of time all the liquid in the inside of the rings has disappeared by diffusion through the agar. We observed circular zones of inhibition of the culture in the dish where no bacteria develops. With a millimeter crystal ruler we determine the diameter of the zone of inhibition. This diameter demonstrates the extent of antibiotic action. In our studies a zone of 24 millimeters of inhibition corresponds to 100 units of antibiotic in each 100 cc of material examined.

All pertinent studies, starting with those of Fleming, express the antibiotic action in units per cubic centimeter. We present our graphs in units per each 100 cc, as all humoral indexes are expressed and in this way the antibiotic action is expressed in whole numbers which are easier to handle than the decimal figures of the older method. Accordingly, all our graphs are made on millimeter paper, each millimeter equals one unit of antibiotic action per 100 cc of the material tested (blood, sputum, etc.)

### *Clinical Considerations*

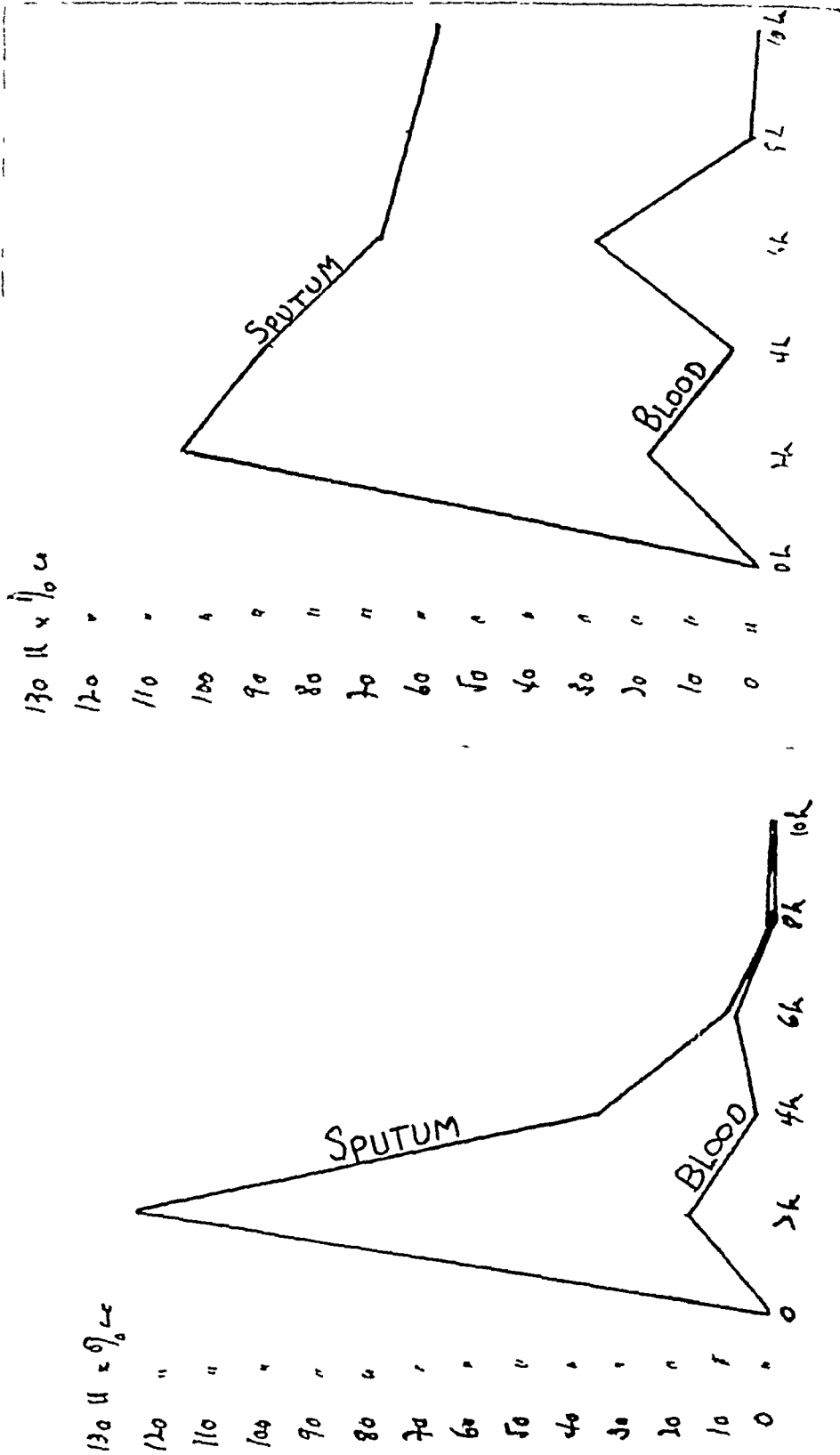
The cases selected were patients who formerly had received oral medication or antibiotics administered parenterally. During the trial of this method, intratracheal crystalline penicillin was used exclusively. No other antibiotic medication was employed at any other time.

Among the cases selected, one patient had a neoplasm with abscess in the middle lobe of the right lung who entered the hospital for an operation. Before his admission to the hospital no diagnosis of lung tumor had been made and suspecting an abscess of the lung, high doses of penicillin were given simultaneously with sulfa drugs. There was no reduction in the amount of bronchial secretions which reached 300 cc in 24 hours and were bloody and purulent. The patient was quite toxic, had moderate anemia with much cough, especially at night and a most aggravating dyspnea. The bronchoscopic examination did not show tracheo-bronchial lesions. Five intratracheal applications were given to him by our method, one every day, using crystalline penicillin in maximal doses of 400,000 units in each application and in solutions of 15 to 20 cc of isotonic saline. We noticed in the first application a definite pharyngeal reflex. We obviated this in the following treatments by giving previously an injection of 10 mg of morphine with atropine. Following the second application, the continuous coughing of the patient was relieved, the expectoration began to diminish and at the end of the fourth application it had come down to 15 cc in 24 hours. The patient's general condition improved and his recovery was maintained for several weeks, when refusing surgical intervention, he left the hospital.

In bronchiectasis we have observed quick reduction of expectoration in 24 hours with a modification of the bacterial flora.

The graphic curve of concentration of antibiotic of sputum and blood simultaneously obtained in this group have been very interesting. We observed that the concentration of antibiotic in the blood was maintained during the first eight hours, fluctuating between 15 and 2 units per each 100 cc. In the sputum, in the same number of hours, the antibiotic action fluctuated between 125 and 35 units per each 100 cc. In case number 5 (Fig 2), multiple bronchiectasis of both lung bases, using always 300,000 units of penicillin at a time, with our method a remarkable difference has been observed in the levels simultaneously obtained from sputum and blood.

In case number 2 (Fig 3), abscess of the vertex of the lower lobe of the left lung cleared promptly under the effect of our treatment. This case, a 31 year old farmer, with a lung affection



FIGURES 2 and 3 Comparative concentration curves of the antibiotic action in sputum and blood

of seven months' duration, was characterized by pain in the flank, high temperature, coughing, abundant purulent expectoration, with asthenia, loss of energy and anorexia. During his second month of illness sulfa drugs were given orally and penicillin parenterally, with no improvement in his condition. The physical examination showed a noticeable oral sepsis, "watch glass" nails and a condensation syndrome at the left-scapular-vertebral zone, with several subcrepitant rales. Mucopurulent sputum showed numerous pyogenic cocci. Its culture revealed the presence of staphylococcus aureus. There was slight anemia, with 15,000 leucocytes, young cells predominating. On bronchoscopic examination we found very fetid secretions originating from the left lower lobe bronchi.

In all, twenty-five intratracheal applications were made in this case, with maximum dose of 400,000 units of penicillin in a solution of 5 cc of isotonic saline. After the fourth application we noticed that the expectoration diminished, coughing at night was less, his appetite and general condition improved. After every application the patient felt better and at the end of the first 20 applications his general condition was good. His expectoration, coughing, fever and asthenia had ceased. He had his normal weight. Nothing important was noticed in the physical examination of the chest. In the x-ray picture we only observed traces of the contrast medium used in the bronchographic examination (Fig 4). In the final culture of the patient's sputum only catarrhalis cocci were observable (Fig 5). Concentration of peni-



FIGURE 4

Fig 4 Pulmonary abscess of the apex of the left lower lobe



FIGURE 5

Fig 5 One month later. Complete resorption of the process



cillin in the blood and sputum curves during treatment was similar to those described in our former observation. This patient was kept in the hospital for several weeks after treatment, without observing any further clinical or radiographic manifestations of the infection.

### SUMMARY AND CONCLUSIONS

1) We have used a technique developed by us for mucosography of the respiratory tract and applied to the treatment of suppurative diseases of the lung.

2) This preliminary report covers a group of cases treated with penicillin which we have used in different concentrations, between 100,000 and 500,000 units dissolved in isotonic saline solution. The application was made daily with progressive increase in the doses of penicillin.

3) We preferred crystalline penicillin because it is better tolerated, the volume used has been 5 cc. Larger amounts show no advantage, for it delays the method, and the patient develops pharyngeal irritation.

4) It is an easy method to use, with no risk or disturbance to the patient. The amount of anesthesia used is very small, atomization of 2 cc of  $\frac{1}{2}$  per cent pantocain solution is sufficient. In some patients we have sprayed without anesthesia, and noticed good tolerance.

5) We perform the atomization continuously. That is, in both phases of respiration, in order that the patient may keep open the glottis to avoid coughing and pharyngeal contractions.

6) We have used the supra and infraglottic technique. We prefer the supraglottic technique because it is better tolerated.

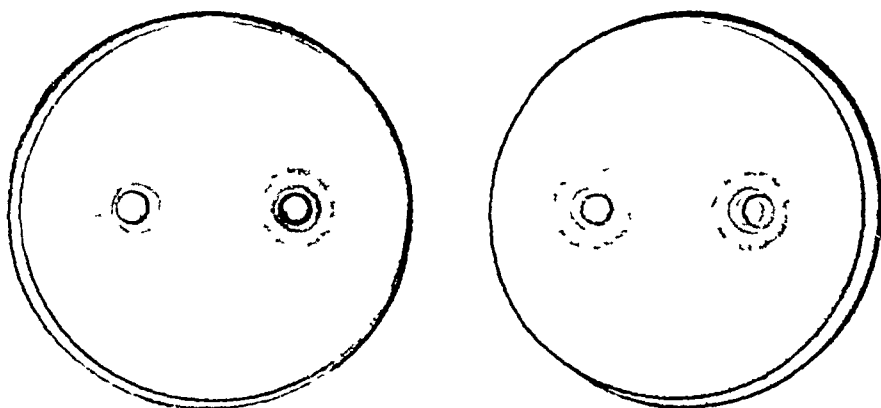


FIGURE 6 Petri dishes showing the different intensity of the antibiotic action of sputum and blood

7) The results obtained are definitely encouraging. We have succeeded in improving and curing suppurative lung conditions some of which were of more than six month's duration and having been previously treated without success with penicillin and sulfa drugs.

8) It is interesting to point out that the simultaneous study of sputum and blood in our patients shows high antibiotic action in the sputum and quite low antibiotic action in the blood. It is easy to see in our graphs that the antibiotic action of the sputum fluctuates between 130 units as maximum and 40 units as minimum, the antibiotic action of the blood fluctuates between 30 units as maximum and 2 units as minimum.

These facts bring forth certain questions which we shall try to explain.

(a) Does the high bacteriostatic power found in the sputum represent the whole penicillin concentration or is it related to any other antibiotic action?

(b) Does the high bacteriostatic action found correspond to accumulative or eliminative action?

(c) Do proteins of the expectoration (mucins, mucoids, etc.), have anything to do with the "delayed effect" in connection with the penicillin deposited in the bronchi?

9) The results obtained point toward the extraordinary importance of the topical action of antibiotics.

10) Finally, with this method we can direct to a certain pulmonary area the highest percentage in volume and concentration of the drug used, which, to our belief is not obtainable by any other method of inhalation used up to the present moment.

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Atomizer described manufactured by the DeVilbiss Company

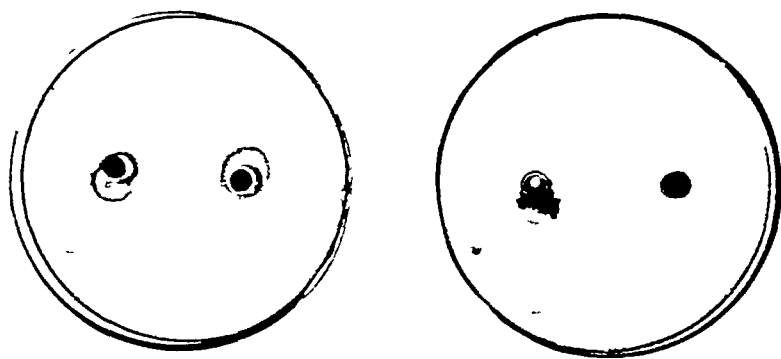


FIGURE 7 Petri dishes showing the different intensity of the antibiotic action of sputum and blood

## RESUMEN Y CONCLUSIONES

1) Hemos empleado una técnica perfeccionada por nosotros para la mucosografía del aparato respiratorio y aplicada al tratamiento de las enfermedades supuradas del pulmón

2) Este informe preliminar incluye un grupo de casos que hemos tratado con penicilina en concentraciones de 100,000 a 500,000 unidades disueltas en una solución isotónica de cloruro de sodio. Se aplicó el tratamiento diariamente, con aumento progresivo en la dosis de penicilina.

3) Preferimos la penicilina cristalina porque es más tolerable. Se ha usado un volumen de 5 cc. Cantidades más grandes no ofrecen ventaja, pues demoran el método y el paciente sufre de irritación faríngea.

4) Es un método fácil de usar que no tiene peligro ni causa desasosiego al paciente. Es muy pequeña la cantidad de anestésico empleada, es suficiente la pulverización de 2 cc de una solución de pontocaína al 0.5 por ciento. Hemos rociado sin anestesia a algunos pacientes y lo han soportado bien.

5) Ejecutamos la pulverización continuamente, es decir, en las dos fases de la respiración, a fin de que el paciente mantenga la glotis abierta para evitar la tos y las contracciones faríngeas.

6) Hemos empleado la técnica supraglótica e infraglótica. Preferimos la técnica supraglótica porque es más tolerable.

7) Los resultados obtenidos son definitivamente alentadores. Hemos logrado la mejoría o la curación en estados supurados del pulmón, algunos de los cuales habían existido por más de seis meses y habían sido tratados previamente sin buen éxito con penicilina y sulfonamidas.

8) Es interesante indicar que, en nuestros pacientes, el estudio simultáneo del esputo y de la sangre demostró una acción antibiótica elevada en el esputo y una acción antibiótica bastante baja en la sangre. Se puede ver en nuestras gráficas que la acción antibiótica del esputo fluctúa entre 130 unidades como máximo y 40 unidades como mínimo, y la acción antibiótica de la sangre fluctúa entre 30 unidades como máximo y 2 unidades como mínimo.

Estos hechos sugieren ciertas preguntas que trataremos de contestar:

(a) ¿Representa el elevado poder bacteriostático del esputo la entera concentración de la penicilina, o está relacionado con alguna otra acción antibiótica?

(b) ¿Corresponde la elevada acción bacteriostática a una acción acumulativa o eliminativa?

(c) ¿Tienen algo que ver las proteínas de la expectoración (mucinas, mucoides, etc ) con el "efecto demorado" de la penicilina depositada en los bronquios?

9) Los resultados obtenidos demuestran la extraordinaria importancia de la acción tópica de los antibióticos

10) Finalmente, con este método podemos aplicar a una zona pulmonar el porcentaje más alto, en volumen y en concentración, de la droga empleada, lo que, en nuestra opinión, no es obtenible mediante ningún otro método de inhalación usado hasta la actualidad

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# Thrombosis of the Main Stem of the Pulmonary Artery Associated with Pulmonary Tuberculosis

## Report of a Case

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Savacool and Chair<sup>1</sup> in 1941, reviewed the literature for one hundred cases of pulmonary artery thrombosis of the main stem or its main branches. In their series of cases nineteen were reported to have had pulmonary tuberculosis as a primary diagnosis. Perusing the literature through to 1946 failed to disclose any further reports of pulmonary artery thrombosis.

The following case is reported because of its many interesting features and because of the diagnostic problem presented by the course and symptoms.

E H, a thirty year old white housewife, entered the San Diego County General Hospital, Tuberculosis Division, on October 26, 1946, with pulmonary tuberculosis confirmed by roentgenograms and sputum containing acid fast bacilli. The patient had been essentially well until nine years before this entry when she first recalled noting dyspnea, with slight exertion, occasionally associated with cyanosis of her face and fingers.

At that time she was seen in the Out-Patient Department of the United States Naval Hospital, at San Diego, where a tentative diagnosis of congenital heart disease was made. Specifically, an interatrial septum defect was considered. Roentgenograms revealed an enlarged right auricle and pulmonary conus. There was a systolic murmur at the base of the heart on the left side of the sternum. The systemic blood pressure and physical examination at that time were otherwise within normal limits. The x-ray films taken on these visits are no longer available for re-examination.

The patient attended the clinic intermittently, noting a gradual increase in the severity and frequency of her symptoms. In February 1945, she entered the United States Naval Hospital following a sudden increase in the above symptoms plus an acute onset of fatigue, fever, sweating, cough and vague chest pain anteriorly.

Roentgenogram taken at that time (figure 1) showed an increase in the size of the upper mediastinal shadow with a bulging density in the region of the pulmonary conus on the left. There were scattered areas suggestive of atelectasis in the left lung field with almost complete atelectasis at the apex. There was also some enlargement of the hilar density on the right. The trachea, in the upper portion of the chest, deviated sharply to the right suggesting the effect of pressure from the mediastinum. The electrocardiogram revealed marked right axis deviation.

The possibility of bronchopneumonia or tuberculosis was considered at that time. Repeated examination of the sputum revealed no acid-fast bacilli and blood cultures on two occasions were negative. The patient was treated with sulfathiazole and required the use of an oxygen tent. Her acute symptoms gradually subsided, over a period of three weeks. The cardiac murmur and a daily afternoon spiking temperature to 101 degrees F orally disappeared as her symptoms subsided. The patient was discharged one month after entry. The x-ray film taken at the time of her discharge showed a considerable amount of clearing of the process in the left lung field with essentially no other changes in the heart or vascular shadows. There was still some residual atelectasis present in the left apex.

Following her discharge from the hospital, the patient continued to note her previous complaints of occasional dyspnea and cynosis. On September 26, 1946, she had a re-check roentgenogram taken at the San Diego County Tuberculosis Clinic. This film revealed, on the right side, a fibrotic infiltration extending out from the hilar region into the second interspace with an area simulating cavitation at the end of the second rib anteriorly. The hilar markings showed some increase in their size and density. The left side revealed some increase in the density previously seen in the first and second interspaces with areas suspicious of cavitation. The contour of the heart and mediastinum were not apparently changed.

The sputum examined at that time was found to contain acid-fast bacilli. The patient entered Vauclain Home on October 26, 1946, following the establishment of the diagnosis of tuberculosis.

The past history included a full term normal delivery preceded by elevation of the blood pressure during the last trimester. She denied symptoms of heart trouble before 1937, joint pains or swelling, chorea,

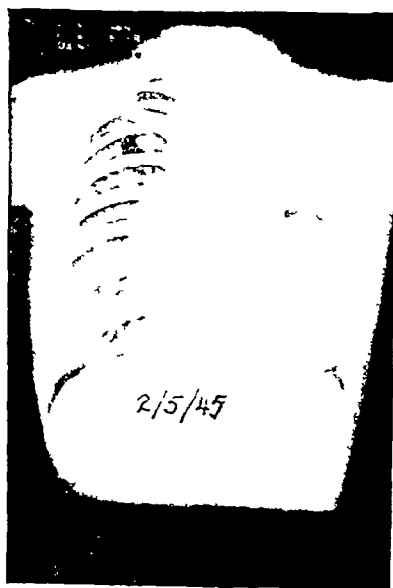


FIGURE 1



FIGURE 2

tuberculosis contacts, venereal disease, or allergy In the family there was no known case of congenital abnormalities or tuberculosis

The physical examination on admission revealed a well developed, poorly nourished, cyanotic, dyspneic white female appearing older than her age and easily upset emotionally Her temperature was normal, pulse 90 and regular, and respirations 22 Blood pressure readings were as follows right arm 118/90, left arm 120/95, leg 110/90

Positive findings included a lag in the excursion of the left side of the chest Anteriorly, at the apex on the left, dulness with breath sounds decreased in intensity and bronchial in quality were noted Posteriorly, at the left apex, dulness with bronchovesicular breath sounds and a few crepitant rales were heard The heart was not enlarged to percussion and no murmurs, irregularities or thrills were present P2 was louder than A2 One observer noted an apical, grade one systolic blowing murmur Her fingers were exhibiting a moderate degree of clubbing

The laboratory tests on admission were as follows urine essentially negative, hemoglobin 103 per cent, WBC 6,600, leukocytes 72, lymphocytes 25, monocytes 3 per cent The Kline and Wassermann tests were negative and the sputum contained acid-fast bacilli

The roentgenogram, dated November 15, 1946 (figure 2) taken soon after admission, revealed no change on the right side On the left side the density in the upper mediastinal region appeared somewhat larger and now simulated a tumor The configuration of the heart was unchanged The electrocardiogram revealed notching of the QRS waves in leads 2, 3 and 4, with inversion of the T waves in these same leads The S wave was depressed in lead 1 These findings were interpreted as representing right axis deviation and right ventricular strain

In January 1947, roentgenogram of the chest with ingestion of barium showed deviation of the esophagus to the right and posteriorly at the level of the fifth, sixth, seventh and eighth thoracic vertebrae, appar-



FIGURE 3

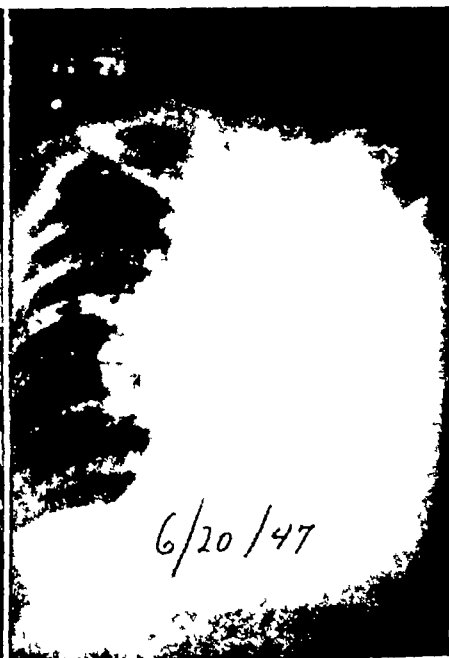


FIGURE 4

ently from extrinsic pressure. Surgery for a possible mediastinal or bronchogenic malignancy was considered at this time but was deferred because of the poor operative risk and prognosis for the patient with active tuberculous lesions in the lung parenchyma.

On February 3, 1947, a Bucky film (figure 3) showed an increase in the size of the density in the right hilar region, with soft infiltration extending out laterally. On the left side there was a fairly well circumscribed density in the upper portion of the hilar region giving the appearance of a tumor mass with a well defined area of atelectasis extending into the lower part of the upper lobe. The interpretation of this increased density was still not clear. During this time, while on bed rest, the patient gradually gained weight. She had an occasional late afternoon spiking temperature to 101 degrees F orally. In April 1947, blood streaked sputum was noted for the first time. Cyanosis was still present and unchanged from that noted at the time of her admission.

On June 17, 1947, the patient felt a sudden pain in her left lower chest which increased in severity during the following three days. This pain was associated with fever, apprehension, increased pulse and cyanosis and the production of small quantities of dark red blood in the sputum. These symptoms, fluctuating in severity, continued until death. Physical examination at the time of the onset of these more severe symptoms revealed dullness over the left side of the chest with absent breath sounds and medium moist rales throughout the left lung field. An x-ray film taken of the chest on June 20, 1947 (figure 4) showed little change in the findings on the right side. The left side was obscured by a homogeneous density except at the extreme apex where some aeration was visible. The heart and mediastinum were shifted to the left. The picture appeared to be that of atelectasis rather than pleural effusion. Attempts at aspiration of the left chest were unsuccessful. Bronchoscopy on July 23, 1947, revealed narrowing of the left main bronchus, apparently due to extrinsic pressure. The orifice of the left upper lobe bronchus could not be visualized. The bronchial mucosa was not remarkable.

In September, re-check laboratory findings included hemoglobin 138 per cent, RBC 7,550,000, WBC 9,750, lymphocytes 19, monocytes 5, eosinophils 1, leukocytes 75 per cent, hemotacrit 80 cc/100 cc, blood urea nitrogen 24.1 mg per 100 ml. On October 5, 1947, the circulation time from arm to tongue with gluco calcium was twenty-three seconds, from arm to lung with ether was ten seconds.

The patient continued in a gradual down hill course, becoming more dyspneic and less rational until October 7, 1947 when she expired with no apparent acute incident terminally. The temperature remained below 100 degrees F and the pulse varied between 100 and 110. The respiratory rate was 20 to 25 per minute up to the time of her death. No peripheral edema or enlargement of the liver was noted. A roentgenogram taken just before death revealed no change in the left side of her chest, however, the lesion in the right midlung field appeared to have been clearing and hardening.

The postmortem examination revealed in the thorax, old pleural adhesions bilaterally. The left lung showed scattered areas of atelectasis especially in the upper lobe with multiple areas of active tuberculosis. The lower lobe was the sight of a massive infarct with thrombotic obstruction of the artery to this lobe. The right lung showed multiple tuberculous lesions especially at the apex with a few scattered thromboses of the smaller pulmonary arteries. The heart presented the picture



of dilatation and hypertrophy of the right side. There was a large laminated antemortem thrombus apparently occluding the pulmonary stem and its two branches extending to the pulmonary semilunar valves. The thrombus was gray in color at the pulmonary artery branches, becoming red in color as it approached the pulmonary valve. The blood clot was firmly attached to the wall of the artery, but when separated there was a clean plane of cleavage with no gross evidence of disease of the large arteries. Unfortunately, no microscopic sections are available.

### *Discussion*

At the onset of her symptoms this 20 year old woman sought medical attention for shortness of breath and blue discoloration of her fingertips. Upon examination cor pulmonale and a basal systolic murmur were found. In the absence of any evidence of pulmonary abnormality a tentative diagnosis of interatrial septum defect was made. Cardiac catheterization would have been of great value in ruling out patent foramen ovale and determining the pressure in the pulmonary circulation which was undoubtedly elevated.

According to Brenner,<sup>2</sup> the above picture fulfills the criteria for a diagnosis of primary pulmonary vascular sclerosis. De Navasquez et al.<sup>3</sup> question the significance of pulmonary vascular lesions in some cases of cor pulmonale due to pulmonary hypertension without apparent etiology and propose the term idiopathic right ventricular hypertrophy. Taft and Mallory<sup>1</sup> believe that this pulmonary hypertension of unknown etiology probably precedes sclerotic changes in the pulmonary vessels. In the absence of any evidence of left heart failure, the markedly prolonged circulation time from arm to tongue as compared to the only slightly prolonged circulation time from arm to lung, point to some peripheral vascular disease in the pulmonary circulation. Brill and Krygier<sup>5</sup> emphasize the significance of cyanosis that is out of proportion to the amount of dyspnea as being an outstandingly frequent finding in pulmonary vascular disease, particularly pulmonary vascular sclerosis. This picture was an outstanding feature of the patient's symptoms, nevertheless that diagnosis remains in the realm of speculation.

In retrospect, therefore, it appears that the patient when first seen had cor pulmonale due to pulmonary hypertension of unknown etiology, possibly due to pulmonary vascular sclerosis.

The acute episode requiring hospitalization in 1945 was considered at that time to be due to a pneumonitis in the left upper lobe complicating a congenital heart disease. Because of the similarity of the roentgenograms taken at the United States Naval Hospital and those taken on admission to Vauclain Home, it is interesting to speculate whether or not the patient had

tuberculosis and/or atelectasis in the left upper lobe in 1945. The former may have been present in spite of repeatedly negative sputa examinations for acid fast bacilli. The latter could have been due to pressure on bronchi by pulmonary vascular thrombi originating at that time.

The time of origin of the pulmonary thrombus raises another point for speculation. The thrombus may have formed in 1945 at the United States Naval Hospital, resulting in atelectasis as pointed out above. On the other hand, this process may not have started until after entry into Vaclain Home where the embarrassed cardio-pulmonary dynamics complicated by tuberculosis in a bed ridden patient may have set the stage for the onset of the process of thrombus formation.

The authors feel that the patient at the time of her first hospitalization, in February 1945, probably had tuberculosis and atelectasis following the onset of the thrombosis. This thrombus continued to grow until the impairment of the blood supply to the left lower lobe was sufficient enough to result in the infarct which occurred in June 1947. Life was maintained until the heart became unable to stand the strain of pumping blood through the pulmonary arterial system so massively thrombosed.

In Dock's<sup>6</sup> explanation of the localization of phthisis he points out that the incidence of apical or subapical lesions of tuberculosis is higher in patients with pulmonary hypotension as compared to the incidence in patients with pulmonary hypertension. This is not inconsistent with the course of events in this case, for the formation of the thrombus in the pulmonary artery may have been expected to have materially decreased the effective pulmonary arterial pressure. This, according to Dock, decreases the oxygenation and impairs function of humoral defenses in the body.

That the thrombosis occurred first in the left pulmonary artery is suggested by the fact that the first changes noted in the lungs were found on the left. Savacool and Charr<sup>1</sup> in their series of 100 cases report only six cases which were interpreted as having thrombosis of the left main branch only or origin of the thrombus in this branch of the pulmonary artery. The relative infrequency of this finding was explained by the longer and more tortuous course of the right as compared to that of the left branch of the pulmonary artery.

### SUMMARY

An interesting case of thrombosis of the pulmonary artery stem and its main branches in a patient with pulmonary tuberculosis is presented with a discussion of the pertinent findings and observations.

## RESUMEN

Se presenta un caso interesante de trombosis de la arteria pulmonar y sus ramas principales en un paciente con tuberculosis pulmonar y se discuten los hallazgos y observaciones pertinentes

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# Platybasia Associated with an Unusual Case of Pulmonary Tuberculosis Report of a Case with Necropsy\*

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Chamberlain's paper in 1939 on "Basilar impression (platybasia)"<sup>1</sup> has stimulated the interest of the medical profession in the study of malformation of the base of the skull and upper cervical spine, an anomaly up to that time receiving very little attention. In this paper he proposed a criterion for the diagnosis of platybasia based on the amount of projection of the odontoid process above a line drawn on a conventional lateral x-ray film of the skull connecting the posterior edge of the hard palate to the dorsal margin of the foramen magnum, the line now being referred to as "Chamberlain's line." Two cases in Chamberlain's<sup>1</sup> series were treated by low occipital craniectomy and laminectomy of cervical segments with definite subjective and clinical improvement of their neurological symptoms.

According to Schueller,<sup>3</sup> on the other hand, the diagnostic features of platybasia are the cephalad bulging of the floor of the posterior cranial fossa around the foramen magnum and the congenital variations of the upper cervical vertebrae.

The case described in this paper is a bizarre one, not only because of the presence of the developmental anomaly of the occipital bone and upper cervical portion of the spinal column, but also in the clinical course of the pulmonary tuberculous disease with its unusual concomitant complications.

## *Case Report with Necropsy Findings*

J.C.B., No 47,620, colored male, aged 25, was admitted to the Veterans Administration Hospital, Alexandria, Louisiana, on December 23, 1946, for treatment of pulmonary tuberculosis. In addition to the usual symptoms of pulmonary tuberculosis, the patient presented the following neurological findings: Excessive sweating limited to the entire left half of his body; fleeting joint pains; loss of the sense of differentiation between cold and heat, and dull and sharp, on the left side. The gait was staggering and unsteady but there was no history of trauma to the head or spine and at no time was there a loss of consciousness or convulsion.

The physical examination disclosed a well developed and well nourished colored male who appeared chronically ill. The temperature, pulse, and respirations were within normal limits and the blood pressure was 120/80.

\*From the Chest Service, Veterans Administration Hospital, Alexandria, Louisiana.

Examination of the chest revealed signs of a bilateral involvement with coarse post-tussive rales scattered throughout the middle portions and bases of both lungs. The above findings were confirmed by x-ray examination of the chest. Routine sputum examinations were consistently reported positive for acid fast organisms. Urine and Wassermann examinations were negative. Sedimentation index was 30 mm in one hour. Complete blood count revealed Hemoglobin 61.4 per cent, Red Blood Count 3,670,000, White Blood Count 8,200, Polymorphonuclears 60 per cent, Lymphocytes 38 per cent and Basophiles 2 per cent, Urea nitrogen 13, Cholesterol 120 and basal metabolism ranging from plus 1.9 to 1.9 per cent.

The Therapy Board recommended that patient be observed for a period of 30 to 60 days. During this period the author bronchoscoped the patient and aspirated a large amount of mucopurulent secretion from both main bronchi, finding no evidence of ulceration or stenosis of the bronchi. The patient's pulmonary condition, however, had not improved on routine management. Subsequent roentgenogram of the chest revealed a definite increase in the lesions in both lung fields and cavitation in the middle portions near the hilar region. Pneumoperitoneum was induced on March 25, 1947.

A transient improvement in patient's clinical and radiological condition was noted under this treatment, but the disease apparently was not controlled. In fact, the patient developed further cavities in the 2nd interspace on the left side and started to hemorrhage (Fig 1). It was decided at this time to induce pneumothorax on the left side in addition to the pneumoabdomen. Patient's vital capacity (2,800 cc), checked prior to inducing pneumothorax on the left side appeared very satisfactory. Electrocardiogram on September 22, 1947 showed sinus tachycardia but no definite cardiac pathology contraindicating combined pneumoabdomen with pneumothorax therapy. Initial treatment of 150 cc of air,



FIGURE 1



FIGURE 2

*Fig 1* Roentgenogram of the chest taken September 10, 1947, shows marked elevation of the diaphragms and a huge cavity in the 2nd interspace on the left side—*Fig 2* Roentgenogram of the chest taken October 7, 1947, shows a collapse of both lungs in addition to an extensive pneumoabdomen.

under high negative pressure, was given on the left side on September 26, 1947 without any ill effect

On October 8, 1947 without any obvious cause, the patient's temperature rose to 104.4° F with a pulse rate up to 120 per minute and respirations of only 22 per minute. The patient was lying in bed quietly but complained of some fleeting pain in his shoulder joint and his left arm. There was no evidence of respiratory distress, nor any orthopnea.

Examination of the chest including fluoroscopy revealed collapse of both lungs with marked elevation of the domes of the diaphragm due to pneumoperitoneum. In other words, this patient had developed a spontaneous collapse of his right lung without noticeable dyspnea (Fig 2). Continuous deflation was started immediately on the right side and patient was placed in an oxygen tent. The following day deflation was stopped because the air was not bubbling through the water trap. The possibility of continuing bilateral pneumothorax was then contemplated, provided that we were not dealing with a congenital mediastinal defect.<sup>2</sup> It was noteworthy that while this patient's temperature was markedly elevated, up to 105° F, with a pulse of 136 his respiratory rate, nevertheless, was of usual frequency, only 18 to 24 per minute, a marked discrepancy between his respirations and his total clinical condition. The patient expired unexpectedly on October 12, 1947.

During the period of hospitalization he continued to have bizarre neurological complaints. The neurological examination disclosed the following positive findings: Pupils central and unequal the right pupil being smaller; a rotary nystagmus bilaterally which became more pronounced on gazing toward the right temporal side; cremasteric reflex absent on the left side; knee and ankle jerks hyperactive on the right side; deep reflexes on the left side markedly diminished; definite sensory changes from the level of the left nipple down and marked sweating of the entire left half of the body.

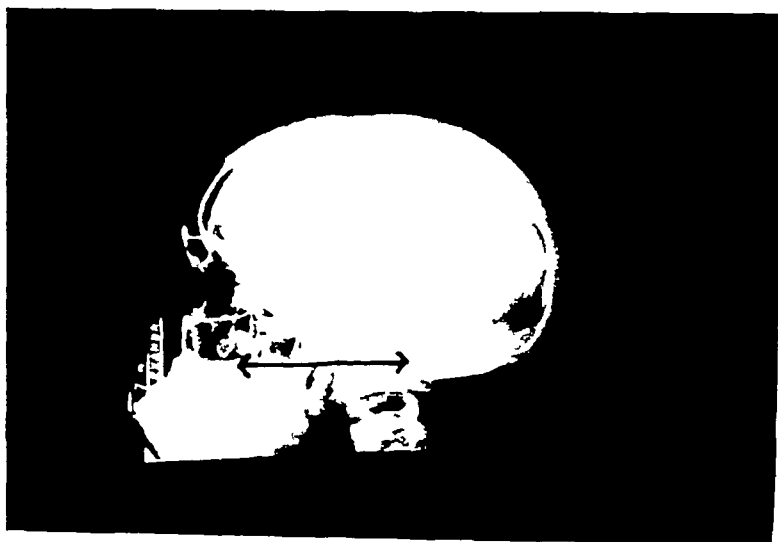


FIGURE 3 Roentgenogram of the skull shows projection of the odontoid process above the line drawn from the posterior margin of the hard palate to the posterior lip of the foramen magnum

These neurological symptoms were suggestive of syringomyelia. The x-ray of the skull (Fig 3), however, showed a flattened and stenosed foramen magnum and projection of the odontoid process well above the "Chamberlain's line," consequently the diagnosis of platybasia was made.

The pertinent postmortem findings were as follows. There was narrowing of the foramen magnum in the antero-posterior diameter and there was elevation of its edge at the anterior rim. The exact anatomy of the atlas and second cervical vertebra was not explored to avoid mutilating the body. There was no protruberance of the cerebellar tonsils through the foramen magnum. The lung findings were in accordance with those demonstrated by x-ray. No demonstrable interpleural communication was present. Histologically nothing of significance was found except for chromatolytic changes in occasional anterior horn cells.

### *Comment*

No other case of pulmonary tuberculosis associated with basilar invagination is to be found in the medical literature. The relationship is coincidental but the neurological changes appear to have masked many of the patient's pulmonary symptoms. The discrepancy between the slow respiratory rate and the febrile clinical course was striking during the entire period of hospitalization.

There is a possibility that we are dealing here with more than one congenital anomaly, both a mediastinal defect and platybasia. This is evidenced by the fact that this patient after the fourth injection of air into his left side developed a spontaneous pneumothorax on the right side without its usual symptoms. The question arose: was there a very slow leakage of air through the mediastinum? This question is impossible to answer positively, because the patient did not survive long enough to permit proof of the defect in the mediastinum. The fact that a mediastinal opening could not be found at autopsy does not rule out its presence because others, such as Smith and Willis,<sup>1</sup> also could not demonstrate the mediastinal defect at autopsy in a proven case of interpleural communication during patient's life.

Our case had a bilateral pneumothorax with collapse of both lungs up to 60 per cent in addition to an extensive pneumoperitoneum, a combination rarely observed in tuberculous patients. There was no noticeable dyspnea at any time in this case which could be attributed to pressure on the respiratory center by some pathological process depressing the respirations. At necropsy there was no demonstrable impression on the medulla or the upper cervical cord due to pressure, nevertheless, histologically there was occasional anterior horn cell chromatolysis signifying a possible degenerative process.

Finally it would not be amiss to stress the fact that thorough search of the skull and cervical spine, especially roentgenolog-

ically, in all suspected cases of spinal cord degeneration showing symptoms of syringomyelia, multiple sclerosis, or other unusual patterns, might disclose many more cases of platybasia

### SUMMARY

1) Platybasia associated with an unusual case of pulmonary tuberculosis is reported and the possibility of a congenital mediastinal defect is also discussed

2) The basilar invagination in this case apparently influenced the respiratory center by a depressing effect on the response of the respiratory rate to stimulation

3) It is advisable that careful search for platybasia be made in every case with degenerative changes of the spinal cord

4) The necropsy in this case confirmed our clinical diagnoses of platybasia and pulmonary tuberculosis with bilateral pneumothorax and pneumoperitoneum

### RESUMEN

1) Se informa sobre un caso de platibasia asociada con tuberculosis pulmonar inusitada y se discute tambien la posibilidad de que existiera un defecto congénito del mediastino

2) En este caso la invaginacion basilar aparentemente influyo el centro respiratorio y causo un efecto depresivo sobre la respuesta a la estimulación de la velocidad respiratoria

3) Es prudente que se investigue cuidadosamente la existencia de platibasia en todo caso que presente alteraciones degenerativas en la médula espinal

4) Es este caso la autopsia confirmo nuestros diagnósticos clinicos de platibasia y tuberculosis pulmonar con neumotórax bilateral y neumoperitoneo

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# Tuberculosis Among Medical and Academic Students

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The problem of tuberculosis among college students has been given careful study at many universities and colleges during recent years. The Tuberculosis Committee of the American Student Health Association has reported each year since 1932 on the tuberculosis activities of a large number of institutions located in all sections of the country. Through assistance rendered by the National Tuberculosis Association, the committee contacts each year all accredited colleges in the nation, approximately 880 in number. More than 300 colleges, having a total enrollment of approximately a half million students, are now conducting case finding programs. The detailed reports from these institutions provide a quite accurate picture of the prevalence of tuberculous infection and tuberculous disease among our student population.

A continuous program of tuberculosis control has been conducted among students at the University of Pennsylvania since 1931. Normal enrollment of full time students has averaged approximately 6,000. During the 15 year period under review in this report, our case finding activities have been directed as follows: the tuberculin test is applied routinely to all entering men students at the time of the required entrance physical examination. Reactors have chest x-ray inspection within approximately two weeks of enrollment. Entering women students, about 200 in number, are x-rayed without preliminary testing. Upper classmen are urged to have chest films annually. Although this is on a voluntary basis, the response has been excellent. X-ray surveys are conducted at the beginning and toward the close of each school year. A required program has been in effect for three groups of students since the inception of our case finding activities in 1931. Medical students receive especially close supervision throughout all four years of training. At entrance to medical school all students are tested with tuberculin by the Mantoux method employing the two standard doses and each student has a chest x-ray, non-reactors as well as reactors. Non-reactors are retested twice during each medical school year and chest x-rays are provided

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for all reactors on an annual basis. During the present school year this plan was revised and now includes retesting of all non-reactors at intervals of two months and chest x-rays for all reactors during the school year. Athletes have also been rather carefully supervised at Pennsylvania. All members of varsity teams competing in intercollegiate athletics are required to have an annual chest x-ray. There are approximately 300 students participating on various athletic teams. The number of athletes found to have significant pulmonary lesions has provided rather convincing evidence of the need for adequate case finding procedures in such a group. The School of Education has also co-operated in a required program whereby their students are x-rayed at the time of entrance and again just prior to graduation. Since all of these young people are presumably entering the teaching profession shortly after graduation, it is important that we rule out the possibility of their being a source of infection in the classroom. The entire cost of the tuberculosis program is financed by a student health fee of five dollars a semester. Approximately 40 to 45 per cent of our students receive chest roentgenograms each year at a total cost of about three thousand dollars. This represents 5 per cent of the department's annual budget and, we believe, is an entirely reasonable expenditure in view of the significance of the tuberculosis problem among young adults of college age. Although the program outlined above assures quite adequate protection for certain large segments of our student body, a considerable proportion of upper class students do not report for follow-up studies each year as we urge them to do.

The incidence of tuberculous infection among college students has showed a steady and significant decline since 1932 when seven colleges reported that 35 per cent of their students were reactors to tuberculin. In 1942-43, among 42,107 students tested at 51 institutions, where at least an intermediate dose of tuberculin was employed, 18.6 per cent were reactors. In that year, thirteen colleges reported the incidence of infection among their students to be less than 10 per cent. Most of these institutions were located in midwestern and northwestern states. It has been shown by Long<sup>1</sup> that a higher incidence of infection prevails among students living on the East and West Coasts than among those in other sections of the country.

At the University of Pennsylvania 48 per cent of the students entering in 1931 were positive to tuberculin whereas the entering class in 1946 showed but 28 per cent to be reactors. This is especially significant in view of the fact that the average age of students making up the 1946 entering class is considerably above that of students entering fifteen years ago. This is accounted for by the

large number of veterans who are now enrolling in our colleges, many of them having been in service for a period of from one to four years. The incidence of tuberculous infection in this group has been somewhat lower than we had anticipated. Although our experience in this connection has been based on a relatively small number of veterans, approximately 4,000, it would appear that men in various branches of the service were, as a group, not unduly exposed to tuberculous infection. The picture might well have been quite different had routine chest x-rays been omitted from the medical examination at the time of induction.

During the past fifteen years a total of 177 students at the University of Pennsylvania has been found to have pulmonary tuberculosis. Of this number, 91 cases of the disease were among medical students and 86 cases were distributed among the students of all other schools. Since medical students comprised but 9 per cent of our total enrollment during this period, it is readily apparent that tuberculosis has presented a special problem to our students of medicine.

Among students on the undergraduate level, with an average age of approximately twenty years, reports from a large number of colleges over a period of years indicate the prevalence of pulmonary tuberculosis to be approximately 2 to 3 cases per thousand. At the University of Pennsylvania we have found approximately 5.7 cases of tuberculosis per thousand students exclusive of those in medical school. This rate applies to the entire non-medical group, including those in the undergraduate schools as well as students of law, dentistry and veterinary medicine. Of the 86 non-medical students found to have pulmonary lesions, 82.9 per cent were classified as minimal, 13.8 per cent were moderately advanced and 3.3 per cent were far advanced. The majority of this group presented lesions which were unstable. In all such cases, leave of absence is recommended and adequate treatment is advised. Readmission to the university is contingent upon evidence of satisfactory treatment and clinical and x-ray evidence of a presumably stabilized lesion. The value of a continuous program of tuberculosis case finding has been amply demonstrated by our experience at the University of Pennsylvania. Early diagnosis is of utmost importance if we are to prevent prolonged disability as well as unnecessary deaths. Only 6 of the 86 students found to have tuberculosis have failed to complete their education on our campus. This is largely due to the excellent and intelligent cooperation which we meet so consistently in dealing with college students. A large number of colleges and universities have had similar experiences. The report of the Tuberculosis Committee of the American Student Health Association for the academic

year 1941-42 shows that 744 new student cases of tuberculosis were discovered at 311 colleges which conducted programs of tuberculosis control. During that year, 319 students resumed their college work having undergone treatment for tuberculosis previously detected at these institutions.

Due to recent technical advances in the x-ray field the cost of surveying a student group has been reduced to a moderate level. With the incidence of tuberculous infection among students being below 30 per cent in most communities, it is of course a distinct economy to use the tuberculin test as a screening method and thus identify those who are infected with tubercle bacilli. Where tuberculin is applied by the Mantoux method employing either PPD or Old Tuberculin, it is quite well established that very rarely indeed will a person with significant tuberculous disease fail to react to the test. Furcolow, Hewell, Nelson and Palmer<sup>2</sup> report that in a series of over 500 cases of tuberculosis, in which they employed graded doses of PPD, more than 99 per cent reacted to the relatively small dose of 0.0001 mg. This is but five times the concentration of the usual first testing dose. They found none of the patients with active tuberculosis to be anergic to tuberculin. Long<sup>3</sup> of the Henry Phipps Institute has also emphasized the constancy with which persons having significant tuberculous disease respond to the tuberculin test. Among 610 cases of pulmonary tuberculosis diagnosed at the Institute during a five year period, only one of this number was a non-reactor. It is noteworthy also that among the 609 reactors, all of whom presented pulmonary lesions, 94 per cent of the white and 96 per cent of the colored patients reacted to the first small dose. A college is therefore justified in limiting chest x-rays to the reactors among their students if costs are an essential consideration. An adequate program of tuberculosis control is therefore available to most colleges, through use of the tuberculin test and x-ray of all reactors, at a cost which should not exceed three hundred and fifty dollars per thousand students.

The problem of tuberculosis among medical students has been rather carefully studied at a number of medical schools both in this country and abroad. Soper and Amberson<sup>4</sup> presented a very complete review of the subject in 1939. The earlier reports in the literature provide quite conclusive evidence that the incidence of tuberculosis in medical students is appreciably higher than in various other groups of comparable age. More recently, investigators have attempted to identify those phases of medical training which may be attended by definite risks of infection and to institute adequate control measures against all possible sources of infection. Several medical schools have succeeded in this manner

in reducing substantially the attack rates of both tuberculous infection and disease

During the past fifteen years 91 medical students at the University of Pennsylvania have been found to have pulmonary tuberculosis among a total of approximately 2,300 students observed during this period. Ten students entered with lesions, thus 81 developed tuberculosis during their medical school training. In 90.1 per cent of students the disease was minimal, in 8.8 per cent it was moderately advanced and in 1.1 per cent it was far advanced. In addition to those presenting parenchymal lesions, there were five students who developed serofibrinous pleurisy. In our experience, tuberculous pleurisy with effusion has developed quite uniformly at approximately five to seven months after the date of primary infection. In all such cases the student is granted a leave of absence for one year and adequate bed rest treatment over a period of months is insisted upon.

The year of medical training in which tuberculous lesions have been detected in our students has followed much the same pattern as reported by other schools. The senior year has accounted for 38.6 per cent of cases, the junior year 49.1 per cent and 12.3 per cent have been found among second year students. The prevalence of tuberculous infection among students entering medical school has shown a decrease in recent years similar to that observed in academic freshmen. In the class entering in 1935 there were 66 per cent reactors to tuberculin, in 1939 there were 59.4 per cent and in the 1946 class 45.0 per cent. Morris<sup>5</sup> reports 58 per cent of medical students as reactors in the entering class of 1932 and 26 per cent reactors in 1940.

In studying the epidemiology of tuberculosis in medical students, nurses and similar groups, the tuberculin test has proved to be of indispensable value. If applied at sufficiently frequent intervals the approximate time of primary infection may be quite definitely established. High infection rates during certain limited periods of training are indicative of an environment which provides undue opportunity for infection. Various reports on the incidence of tuberculous infection in medical students and nurses indicates almost without exception a rate of increase from year to year which is well above that of the general population. Boynton<sup>6</sup> compared the incidence of infection in students in the college of education, student nurses on a general hospital service and student nurses on a special tuberculosis service. The infection rate was 100 times as great in those on a general hospital service as in college of education students and 500 times greater among those on a tuberculosis service. In the large general hospitals of our eastern cities a very high percentage of non-reactors among

nurses acquire infection during training Israel, Hetherington and Ord<sup>7</sup> report on their observation of 637 nurses followed through three years of training at the Philadelphia General Hospital Of 277 non-reactors on admission to training, 48 per cent became reactors during the first four months By the end of the third year all of the originally negative group had become positive Sixty-eight nurses or 10.6 per cent developed tuberculosis At Bellevue Hospital in New York, Riggins and Amberson<sup>8</sup> found that close to 90 per cent of non-reactors among nurses converted during their three years of training Up until quite recently there were but two or three members of each of our senior classes in medicine who remained negative to tuberculin up to the time of graduation In 1945-46 however, the picture was as follows Fourth year, 70 per cent reactors, third year, 64.4 per cent, second year, 55.8 per cent, and first year, 43.6 per cent A recent report by Brean and Kane<sup>9</sup> dealing with tuberculosis among Harvard Medical School students presents several features of interest In the 1932 entering class, 78 per cent of the students were tuberculin reactors whereas in the 1944 class there were 45 per cent reactors During the period 1940-45 the attack rate of tuberculous infection was practically the same for students of all academic years, 12 to 13 per cent annually The incidence of pulmonary tuberculosis in the medical classes of 1926 to 1932, during which period there was no organized case-finding program, was 0.9 per cent Following the adoption of a program providing for routine tuberculin testing and annual x-ray of reactors, the classes of 1937 to 1943 showed an incidence of tuberculosis of 2.2 per cent Their observations relative to the development of tuberculosis among those entering as reactors as compared with non-reactors led them to conclude that "the nature of the tuberculin reaction on entry had little influence on the development of active pulmonary tuberculosis in medical schools" They emphasize the need for continuous and adequate supervision of young adult groups who may have repeated contacts with tuberculosis by the following observation "The adoption of a program in which surveys are made at intervals more frequent than once a year led to the elimination of almost all symptom-detected cases and of all major lesions It is our belief that a semiannual examination represents the maximum interval for routine re-examination by x-ray and tuberculin tests, not only for medical students but also for nurses and interns"

During the past ten years the annual attack rate of pulmonary tuberculosis among our medical students has varied between 2.1 per cent and 0.38 per cent The higher rate is based on 11 new cases discovered in 1938-39 while the lower rate prevailed in each of the last two years, with two new cases in each year During

this ten year period 57 students developed tuberculosis among 1,700 students under observation, an incidence of 3.3 per cent. The last six years, however, have witnessed considerable improvement, the incidence during this period being 1.8 per cent. The lowered rates of infection and disease during the past few years have followed the adoption of various measures planned by a faculty committee after careful study of the problem over a period of years.

The various clinical and laboratory courses which have been considered at various schools as potential sources of infection to students are the following: Medical clinics, where known, open cases of tuberculosis are used for clinical teaching, physical diagnosis instruction, employing advanced cases of tuberculosis for the demonstration of abnormal physical signs, the pathology laboratory, in the demonstration and examination of gross specimens and the autopsy room with repeated attendance at necropsies on tuberculous subjects, the bacteriology laboratory, if work with virulent tubercle bacilli is required. There are also, of course, casual contact exposures which may be encountered during the clinical years through examination of undiagnosed cases of tuberculosis on various ward services and in the out-patient departments. At Pennsylvania we have attempted to reduce by every possible means the exposure of students to known sources of infection. It was observed that new lesions were detected in third year students more frequently than in other classes. And since most of these were discovered during the first few weeks of the school year, it seemed obvious that if the disease were due to superinfection from exogenous sources, such infection had probably occurred some months previously. Our records showed that there was a significantly higher conversion rate among second year students than among students of other classes. It was apparent, therefore, that the second year offered at least somewhat greater opportunity for reinfection than any of the other three years. Activities in the second year of medicine which provided possible contacts with tubercle bacilli were chiefly the courses in physical diagnosis and in pathology. In the former it was not unusual for students to spend repeated and prolonged sessions in the examination of patients with advanced tuberculosis. This practice has been discontinued. The department of pathology now uses only fixed specimens for laboratory demonstrations. Autopsy room technique was given careful consideration and several changes made for the protection of students. These included more adequate facilities for the washing of hands and the immediate discarding of contaminated gloves, gowns, and aprons.

Hedvall,<sup>10</sup> of Lund University, observed the frequency with which

primary infection in medical students coincided with the course in general pathology. Thorough and repeated examinations of autopsy rooms were made for the presence of tubercle bacilli. He reports that "in spite of all precautions as regards cleanliness during the post-mortem examination, tubercle bacilli were discovered in the rooms and on different objects when an examination was made twenty four hours after a necropsy examination of a person with tuberculosis." More stringent precautions for disinfecting autopsy rooms were taken and the number of autopsies attended by students was greatly reduced. Following the adoption of this plan they found that for the first time in their experience "all students who were non-reactors at the beginning of the course were also negative at the conclusion of the course." This observation, however, covered only two classes which completed the course under the new plan of reduced exposure.

Meade<sup>11</sup> of the University of Rochester Medical School recently reported a very thorough study of this problem and a program for its correction which has proved to be highly effective. Before instituting a case finding program in 1937, the known annual incidence of tuberculosis among their students was 0.9 per cent. By October 1941 their program provided for routine chest x-rays three times during the school year and in March 1943 tuberculin testing and chest x-rays were stepped up to four times a year. The average annual incidence of disease for the period 1937-42 was found to be 3.2 per cent, with a high of 5.0 per cent being reached in the school year 1939-40. Their investigation of probable sources of infection revealed that over a period of years an average of 52 per cent of students were reactors to tuberculin at the beginning of the second year whereas 91 per cent were reactors at the completion of the year. Thus 81 per cent of non-reactors acquired primary infection during the second year of the medical course. The only courses offered during this period in which students had known contact with tubercle bacilli were bacteriology and pathology. They felt that the former offered little, if any, degree of risk. With the cooperation of the department of pathology it was therefore agreed upon to eliminate all contacts with tuberculous materials in autopsy rooms and laboratories during a trial period. The program provided that no student would participate in known tuberculous autopsies, that students were to be dismissed from participation as soon as unsuspected tuberculosis was found at autopsy and no tuberculous materials were to be handled by them. Following the adoption of this policy most striking reductions were observed in both infection rates and the incidence of tuberculous disease. Students completed the first two medical years with only 8 per cent of non-reactors now becoming



positive There have been no cases of tuberculosis among the students of two classes which have been followed through to graduation subsequent to the revision of practices in the pathology course

Meade's experience relating to the development of tuberculous disease among students entering medical school as non-reactors is of special interest Among 138 students who were reactors at entrance, there were four, 2.89 per cent, who developed tuberculosis before graduation Of 175 students negative on entry who became positive during training, there were 27 cases of tuberculosis, 15.4 per cent of the group In this series of cases the average interval between the first known positive test and the detection of a pulmonary lesion was 7.6 months This experience is in keeping with that of other investigators

Morris,<sup>5</sup> reporting on the observation of 449 women medical students over a period of twelve years, sums up her experience as follows "An infection rate of 100 per cent, x-ray evidence in 16.7 per cent, a clinical morbidity rate of 12.5 per cent, a case fatality rate of 10.7 per cent and a mortality rate of 1.3 per cent developing in a stronghold of medicine with facilities readily available certainly constitutes a challenge of sufficient magnitude to interest the entire medical profession in a survey of conditions in other medical educational institutions and hospitals" Morris observed the time relation of tuberculin conversion and the subsequent development of pulmonary lesions in a group of 38 students In 22 of these there was x-ray evidence of disease within six months of the conversion date and in 12 others the interval was under one year Israel<sup>7</sup> and his co-workers report that 12.3 per cent of nurses who were non-reactors at the beginning of training developed clinical tuberculosis as compared with 9.4 per cent developing lesions among those originally reactors They call attention, also, to the earlier development of disease among non-reactors They state "The time occurrence of tuberculosis differed distinctly in students tuberculin negative on admission and those who were tuberculin positive In the former group the lesions developed considerably earlier and the attack rate fell off sharply during the third year Among students reacting to tuberculin on admission the attack rate rose very slowly and reached its maximum in the third year of training" Zacks and Sartwell<sup>12</sup> studied the inmates of an institution for the feeble-minded and found a higher incidence of tuberculosis among non-reactors This they attributed to conditions which favored heavy exposure, as indicated by high infection rates Their comment on this phase of the problem is as follows "One may expect that, in persons whose environmental contact with tuberculosis is heavy and con-

tinuous, most of the cases will develop among non-reactors" Similar findings are reported by Heimbeck and others in numerous publications from Oslo, Norway, dealing with medical students and nurses who have spent considerable periods of training on various tuberculosis services. The foregoing reports seem, therefore, to present a rather definite pattern. This may be summed up as follows. An environment which provides for repeated, and at times, heavy dosage of infection with tubercle bacilli invariably contributes to high infection rates among young adults. If such exposure extends over a considerable period of time, reinfection may follow closely upon a primary infection which has produced a high degree of hypersensitivity to tuberculoprotein. Under these conditions, pulmonary lesions of the reinfection type frequently develop within relatively short periods following primary infection. The size of the dose of tubercle bacilli undoubtedly plays a major role in the production of such a picture. This is emphasized by Rich and McCordock<sup>13</sup>. Commenting on the role of immunity and allergy in tuberculosis they say "Tubercle bacilli introduced into the body of an infected animal appear to be held locally, i.e., to spread less rapidly from the site at which they first lodge and furthermore, they are undoubtedly less able to survive than they are in the tissues of a normal animal. The infected body becomes changed in some manner which renders the bland protein of the tubercle bacillus capable of acting upon the tissues as a powerful irritant or poison. As a result of the change, the cells of the allergic body are more extensively damaged and killed by a given amount of tuberculoprotein than are the cells of the normal body. More extensive damage and death of cells and more extensive, acute inflammation, constitute, therefore, the local, visible expression of the action of allergy."

In our observation of medical students during the past fifteen years the appearance of a parenchymal lesion of the reinfection type following closely upon primary infection has been encountered but rarely. In only one student has this interval been under one year. Moreover, a higher percentage of our students who entered as reactors have developed pulmonary lesions of the reinfection type than those entering as non-reactors. Gerberding<sup>14</sup> has reported similar findings in his observation of primary infection in young adults in Germany. He states "The morbidity of those who have a negative tuberculin test is lower in Germany than in the more northerly located European countries." He is not in accord with those who claim that a high degree of protective immunity is conferred by primary infection. "Although it is no longer generally accepted that the healed primary tuberculous focus causes a specific immunity, the author is inclined to believe

that the healed primary focus provides some protection against small, occasional new infections and, on the other hand, is maintained and renewed by such infections" Myers<sup>15</sup> and his co-workers carefully observed the results of primary infection in a group of 423 student nurses and 134 medical students. Of this entire group of 557 young adults, all of whom became reactors to tuberculin while under close supervision, only three developed early symptoms which might be attributed to tuberculosis. All three developed erythema nodosum. Twenty six students showed x-ray shadows which were interpreted as representing the parenchymal involvement due to primary infection. Regarding their experience as to the significance of primary infection acquired in young adult life, they comment as follows: "The primary complex as it develops in the body of the adult is a benign disease and apparently is of no more clinical significance than the complex which develops in the body of the child." Our experience with relation to primary infection acquired by medical students has been quite similar to that reported by Myers. Four students developed pulmonary lesions which we considered to be of the primary infection type. These were small, sharply delimited areas of a nodular type of density which made their appearance at about six to eight months after the development of sensitivity to tuberculin. In our experience, these have a tendency to persist over long periods of time and do not clear as readily as the exudative type lesion of reinfection. Since there is danger of breakdown and spread from these primary pulmonary foci they should be kept under closest scrutiny including frequent chest roentgenograms. The picture presented by primary tuberculous infection in adults differs in several important respects from that so frequently seen in infants and children. Pulmonary involvement is apparently much less frequent in the adult, the parenchymal lesion is more frequently localized in the upper portions of the lung and is practically never encountered as the massive, pneumonic type of process so characteristic in early childhood. We have followed several hundred students for periods up to several years following primary infection, with chest films at rather frequent intervals, and we have never seen the pronounced hilar node enlargement proceeding on to calcification which is so common in infants and young children.

The specificity of the tuberculin test has been well established although very few studies have been conducted with results that would indicate any real significance on a quantitative basis. However we have observed a small number of students in whom markedly increased sensitivity to tuberculin was followed in a few months by the development of significant pulmonary lesions. Some of our students are rather apprehensive about the dangers

of contracting tuberculosis and come to us as often as every two or three months for retesting with tuberculin and chest x-rays. We have, therefore, had the opportunity to retest frequently students who were slightly sensitive only to the larger doses of tuberculin. The following case history is one of several such experiences which have been of particular interest. A student had normal chest films in his first and second years during which time he was negative to the usual first test dose of 0.01 mg. old tuberculin, but gave a one plus reaction to the second dose of 1.0 mg. old tuberculin. At the beginning of his third year he had two courses, one following the other, in which he stated there was definite contact with advanced, open cases of tuberculosis. On October 5, 1936 he was again negative to 0.1 mg. and slightly positive to 1.0 mg. of old tuberculin. Chest x-ray inspection on November 13 was again negative. On November 21 he reported for another tuberculin test because of his continuing exposure to tuberculosis. The 0.01 mg. dose of old tuberculin now produced a strong three plus reaction. It was recommended that he have chest x-ray at intervals of six to eight weeks. He did not return, however, until April 6. At this time x-ray revealed a small, left apical lesion and tubercle bacilli were demonstrated in the sputum two weeks later. We are now following rather closely a considerable number of students who react only to the larger dose of tuberculin. By frequent testing, we hope to determine what proportion of students may exhibit a marked increase in sensitivity, especially following known exposure to tuberculosis. Frequent x-rays of those showing this change should throw considerable light on its significance in the subsequent development of tuberculous disease.

### SUMMARY

Programs for the control of tuberculosis among college students are now being conducted at several hundred institutions. The incidence of tuberculous infection among entering students has shown a very significant decrease during the past fifteen years. In most sections of the United States less than 30 per cent of undergraduate students react to tuberculin and in many areas, less than 20 per cent.

During the past fifteen years a continuous program of tuberculosis case finding at the University of Pennsylvania has resulted in the detection of 177 students with pulmonary tuberculosis. Medical students and nurses frequently show surprisingly high rates of infection during their training, a condition which invariably gives rise to a high incidence of disease. Tuberculin tests applied at intervals of two months provide a most accurate method of determining those phases of medical school training

which offer the greater risks of tuberculous infection Chest roentgenograms should be provided for all medical students who are reactors to tuberculin at least twice during each academic year

### RESUMEN

Actualmente varios cientos de instituciones cuentan con programas para el control de la tuberculosis entre los estudiantes de colegio La frecuencia de la infección tuberculosa entre los nuevos estudiantes ha mostrado una disminución muy significativa durante los últimos quince años En la mayoría de las secciones de los Estados Unidos menos del 30 por ciento de los estudiantes aun no graduados reaccionan a la tuberculina y en muchas zonas, menos del 20 por ciento

Durante los últimos quince años un programa continuo para el descubrimiento de casos de tuberculosis en la Universidad de Pennsylvania ha resultado en el descubrimiento de 177 estudiantes con tuberculosis pulmonar Los estudiantes de medicina y las enfermeras frecuentemente presentan durante su adiestramiento índices de infección sorprendentemente elevados, lo que invariablemente produce un alto porcentaje de enfermedad

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# The Place of Psychiatry in the Program of a Tuberculosis Hospital\*

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Tuberculosis is an illness in which the scale of emotional involvement is of particular interest. Disturbance of feeling is promptly and deeply aroused. The response of the patient is partly the reflected shadow of social myth and superstition, it is partly an awareness of the personal and social implications of the illness itself, and partly it represents an emergence of latent, specifically individual infantile and neurotic potentialities.

By its very nature, the illness imposes upon the patient the threat of violation of the integrity of his personality, and changes the meaning and direction of his life course. It is a crippling illness in a real sense, since there is so high an incidence among people in the productive years of life. The social stigmatization associated with tuberculosis places the patient in an outcast situation, and the nature of hospital treatment, with its enforced inactivity and dependency, engenders feelings of parasitism and uselessness. Again, where surgical procedures are carried out, feelings of mutilation, of damage to the body image, are common and highly disturbing. In each phase of the illness, there are special reactions of anxiety which present important problems of management and care.

The psychiatric program at National Jewish Hospital, in its steady expansion, has revealed a growing awareness of the major importance of psychological factors in the onset, course, and outcome of tuberculosis. Initiated in 1936 by Dr. Charles J. Kaufman, the previous medical director, it has demonstrated that psychological understanding and management are indispensable in the care of the tuberculous patient.

In previous papers, we have discussed some of the psychological problems encountered in the tuberculous patient. In this paper, we shall review the problem of the administrative integration of psychiatric service in a tuberculosis hospital, from the standpoint of certain general principles in applied psychiatry, as well as

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the specific ways in which psychiatric time is used in relation to these principles

The first general consideration is that the patient in the hospital finds himself in a situation of group living with relations to the staff which are defined by hospital rules and routines, and by the psychological nature of medical authority. As a result, the role of the patient resembles the dependent situation of the child, and the staff role the position of the parent in a family group.

An important aspect of this staff-patient relationship is its ambivalent character. The patient's dependence on the staff for the gratification of his needs for affection and care makes him particularly vulnerable to feelings of frustration and resentment. The expression of such feelings often leads to patients being described as uncooperative and to their discharge as disciplinary problems. The hostility of the patient is thus met not with an effort at an understanding of its origin, but with counter-hostility from the hospital authorities.

A hospital psychiatric service may be oriented to direct work with the patients, and may then be described as "patient-centered," or it may be oriented to the task of helping the people who carry the actual day-by-day responsibility for the patient, and this then is a "staff-centered" psychiatric service.

Our experience has been that a "patient-centered" psychiatric program in a tuberculosis hospital tends to be sterile, unproductive, and unrewarding. It has little or no value as a technique of staff development in comprehensive patient care, it makes no contribution to the problem of the hospital management of the patient, it leaves to one side the possibility of bringing into being a psychologically-enriched view of the illness, and of the experience of the patient with his illness and its treatment.

The attitudes, prejudices, intolerances, and personal problems of the hospital staff are as much a part of the patient's experience with his illness as what goes on in his chest, or for that matter, what goes on in his personality. If medical care is not correlated with consideration for the social and psychological situation of the patient, it reduces itself to technical absorption and tends to lose the dignity of a professional character. Psychiatric care may fall into the same pitfall of technical isolation.

Most psychiatric programs in tuberculosis hospitals begin on a "patient-centered" basis. The service is offered to individual patients or to groups of patients, with attention focused on intrapsychic process, very often without consideration of its relation to hospital living. Most psychiatric problems in the tuberculosis hospital do not require specialized psychiatric treatment but may be handled through the understanding and proper orientation

of the staff. On the other hand, a "staff-centered" program does not exclude direct treatment of the patient by the psychiatrist in the small percentage of cases where it is indicated.

We have found that, given the opportunity, members of the staff are eager to discuss the problems they have with patients, are eager to enlarge their own understanding, and are able to find comfort, reassurance, and help through discussions with the psychiatrist or the psychiatrically oriented social worker which meet them at their own level of thinking and feeling.

In the hierarchy of staff members as parental figures, the physician occupies a special role because of his key responsibility for the medical destiny of the patient. Actually patients are always bringing or wanting to bring their personal problems to the attention of the physician. There are many doctors who are talented in the intuitive grasp of the personal problems of their patients, and deal with them understandingly and successfully. Because of the special nature of the doctor-patient relationship, the patient may often be able to confide more directly and more intimately to the doctor who is responsible for medical management than to any other person, including the psychiatrist.

However, it is misguided, and even somewhat naive to expect a physician who is untrained in psychiatry to be able to understand the personality structure of the patient, the dynamics of his reaction to his illness, his medical care, and his hospital experience, or the interplay of personality in the staff-patient relationship as it affects the patient's response. While we have found considerable variation in psychological flair and capacity among our staff physicians, there is little doubt that the opportunity to share in the psychiatrist's thinking and to make use of the psychiatrist's time for consultation on cases is of great value.

Certainly the physician without thorough psychiatric training and particularly without extensive training in the discipline of psychotherapy runs the risk of allowing the patient to develop unconscious, intense emotional reactions which must be handled to avoid psychological damage. These are reactions such as acute episodes of hostile, irritable, spiteful behavior, or completely submissive attitudes of devotion and love, like the "crushes" of the adolescent, sensitizing the patient to every gesture and imagined whim of the doctor. These reactions are the result of retained infantile impulses, which are generally kept under cover but which may break through in any intensive doctor-patient relationship. As a result of his training, the psychiatrist is able to recognize these manifestations, and to make use of techniques which will either keep them under control or allow them to be dealt with skillfully as they appear.



We see the role of the psychiatrist, then, as that of participant in the common effort of general care of the patient, as a member of the clinical team of the hospital, in which each professional group, including the physician, nurse, social worker, psychologist, occupational therapist and vocational adviser, contribute from their own professional training and experience, and by the use of their own professional methods, to the welfare of the patient.

From the point of view of the psychiatrist, the contribution of the psychiatrically oriented social worker is particularly important. In addition to rendering direct social and personal services, the social case worker is in a position to offer the patient a unique continuity of interest in relation to such problems as his separation from family, adjustment to hospital routines, family needs, and preparation for re-establishment in the community. Furthermore, the social worker has received extensive instruction during her school experience in modern, dynamic, psychiatric concepts, and has, at this point, more training than the physician in the observation and understanding of personality processes. Psychiatric services can therefore be most effectively deployed in terms of the concept of participant psychiatry in hospital settings where psychiatrically oriented social service is soundly developed.

From the vantage point of this general introduction, we shall now discuss the specific ways in which psychiatric services are employed at the National Jewish Hospital. There are four main types of activity, including consultation, teaching, treatment, and research. These activities are all inter-related and interdependent, and all represent important elements in a program of psychiatric services in a tuberculosis hospital.

*Consultation* In many ways, this is the most basic contribution of the psychiatrist. The two main groups to whom such consultation is available are the physicians and the social workers, and these are the staff persons who deal most directly with the personal problems of patients. The psychiatrist may interview the patient and then discuss the case with the interested staff member, or more commonly, the discussion is on the basis of case material presented by the doctor or worker. Since the emphasis is on helping the staff person in his problems with the patient, recognition must be given to the person's own way of dealing with interpersonal problems, the extent of his understanding, his limitations in understanding, his own feelings about the patient's behavior, i.e., what it means to him, whether he is over-identifying with the patient's problems, or rejecting the patient and unable to accept the problems. These are all considerations which influence the psychiatrist's activity, and it will be of interest to the psychiatrist to explore how far the staff person can go in recognizing

his own role in the relationship, to what extent he can be helped with prejudicial attitudes, and most important, to attempt to relieve anxieties which he has developed in his dealings with the patient

*Teaching* Although consultation is the core of the psychiatric service, a program of education in psychiatric thinking is carried out through seminars and group discussions, with the object of procuring acceptance from the staff of certain basic principles, for example, (1) that behavior is always meaningful, motivated, and dynamic, i.e., a product of interaction of personality forces, (2) that there is an intimate relationship between the patient's emotional life and what happens to his disease, (3) that the interests of comprehensive medical care require that proper consideration be given to the patient's personal problems and his emotional difficulties, and (4) that the patient's experience in the hospital, in his relations to staff, is important to the course of his illness

Psychosomatic seminars are held regularly, and are attended by all members of the professional staff. In addition, courses in psychosomatic problems are given to student and graduate nurses and to occupational therapists by the chief social worker

In passing, it might be mentioned that an educational program is also carried out for patients. Its purpose is to orient patients at every phase and in every respect of their disease and its management, including consideration of emotional attitudes and problems, its productive results are described in another paper

*Treatment* Our general policy has been to offer direct psychotherapy to any patient who expresses an interest in such treatment. The actual number of patients in psychotherapy is probably greater than at most tuberculosis hospitals, since many patients are referred for the purpose of receiving direct psychiatric treatment, as well as for the care of their tuberculosis. At the present time, there are about twenty patients in psychotherapy. There are some who are being treated by the consulting psychiatrists in connection with the research project, some are seen by the staff psychiatrist, and others are treated by psychiatrists from the Mental Hygiene Clinic of the University of Colorado Medical Center

A special aspect of psychotherapy is that of helping the patient to adjust to his hospitalization. A number of patients are admitted with marked evidence of reactive anxiety, expressing fear for their future, fears about their family and fears about surgery. There is often marked relief of anxiety after a few psychiatric interviews. We have found that a good deal of this work could be done by social workers under the supervision of the psychiatrist

In some instances, for example, in four cases of homosexuality being seen by the staff psychiatrist at this time, the training and skill of the psychiatrist are needed to help the patient to accept the limitations imposed by hospitalization and to learn to live with his psychiatric problem during the period of treatment.

Problems which require particular understanding are those in which the patient displays marked responses of hostility, dependence, and anxiety. Very many instances of aggressive, defiant, resistive, and negativistic behavior may become acceptable and manageable when understood in terms of these basic responses, which are in constant interaction with one another. Anxiety, for example, may lead to an increased need for evidences of interest and affection from the staff, or to feelings of frustration, with mounting irritability and aggressiveness.

The very situation of dependence which is inherent in being hospitalized creates anxiety in some patients. Others have always had difficulty in accepting authority, and react to routinized and restricted living with hostile feelings, which in turn may produce anxiousness and fears of rejection.

The patient who is constantly seen out of bed, who seems to delight in a display of butt-filled ashtrays, who seems to swagger in an attitude of challenge, may be reacting to feelings of insecurity, testing the physician to gain reassurance that he is accepted anyway, seeking love and care through his devious and painful distortions of behavior. Similar behavior may be found in other patients whose feelings of tension and reservoirs of guilt can only be relieved by provoking criticism and punishment from the staff.

These few examples illustrate the importance of obtaining a clear and full picture of the personality of the patient presenting emotional or behavioral problems. They add weight to our premise that understanding of personality factors is often essential in formulating a comprehensive program of medical care for the patient.

While direct psychiatric treatment has a real place in the tuberculosis hospital, it is also important to stress the need for individualized understanding of all patients, and for psychotherapeutic orientation of the hospital program as a whole. From this point of view, routines and regulations, policies and procedures should be constantly re-examined and reviewed, and subjected to revisions which seem necessary in the interest of protecting the emotional situation of the patient.

*Research.* A continuous process of enquiry into the relations between tuberculosis and emotional reaction is as essential in the maintenance of high professional standards as is research

in the biological and clinical aspects of tuberculosis. For the past year, a pilot study in psychosomatic inter-relations in tuberculosis has been under way. We have tentatively concluded that there are no specific trends or patterns of emotional disturbance to be found in the patient with pulmonary tuberculosis but that a statistically significant percentage were in states of emotional upset in relation to current life situations in the period preceding the physical breakdown. There is also some evidence of a positive correlation, as in essential hypertension, between the status of hostility in patients and the course of their illness.

### SUMMARY

We would emphasize that all of the aspects of psychiatric service which we have outlined above are important, and need to be effectively integrated in the development of a sound program of psychiatry in a tuberculosis hospital. For example, we would regard it as a forlorn hope to attempt to carry out a limited teaching program in the psychiatric aspects of tuberculosis, and expect that it could then be applied without the continued participation of a psychiatrist and psychiatrically oriented social worker.

We therefore stress the need for continuity of a program as we have outlined it, and also the need to orient such a program on the basis of a concept of participant psychiatry.

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## D I S C U S S I O N

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You have heard a very interesting paper on the relationship between tuberculosis and psychiatry in a big hospital. I shall discuss the subject from the general aspect of all patients with tuberculosis, those who are cured and those who are not, and the approach necessary to keep them happy and satisfied. I have stressed for years, in lectures to doctors, students and nurses, that tuberculosis is a three-fold entity, primarily a pathology, next a sociology, and third, a psychology.

I might cite a case with an interesting psychological slant. This woman was in a sanatorium—not as large as the National Jewish, but it had 60 beds and a considerable number of patients. Her husband said to me one day that he had attended one of Aimee McPherson's sessions, had seen her cure a child of deafness and wanted to take his wife to see her. I presume you all remember Aimee—she was an evangelist who worked entirely on personality

I said "Your wife is getting along very well, has she no faith in me?" He said "She has perfect faith in you" I said "What can Aimee McPherson do that I cannot do? I have as much education as she, and more I have medical training which she has not" He said "Yes, but she cures through faith in Jesus Christ" I said "Well, why can't I do that?" and he said "You know I never thought of that!"

The treatment of the family of a patient with tuberculosis and the solving of their problems is just as important as treating the patient. When a man has tuberculosis and a wife and four children at home, and no money to feed them, I can't see that psychiatry and psychology will do any good. That man needs a few real dollars to take care of his family, therefore the approach is not to try to cure the man's emotional state but to see that somebody supplies food for the family. Another angle is one in which there may be no economic problem, where a man is doing fairly well and his wife and daughter come to see him three times a week and stand at the bedside and cry. There is no use telling that man not to be emotional, the thing to do is tell his family not to be emotional.

There are numerous angles. A young man, let us say, 34 years old, married, has had tuberculosis for fourteen years, undergone a four-stage thoracoplasty and still is not well. I would feel emotional under those circumstances. How can we explain to that patient that the future holds some promise for him? I don't believe any psychiatrist can handle that. Or consider the case of a woman who gets well, whose husband is so afraid that she will infect his children that he makes her live apart from the family. It isn't the patient who needs treatment, it is the family who must be given the understanding that the patient is now well and will not infect the children. There are certain nationalities, Italians and Greeks and Portuguese, upstanding people in the community, who still have this awful fear of contagion. Then there is the angle where the patient is constantly fearful that he or she will infect the children. Those are real problems that we, as doctors, not as psychiatrists, must face.

I do not believe it takes a psychiatrist to understand these patients. I believe the prime object of psychiatry, which I recognize as a great science, whether in a hospital or outside, should be to train doctors and social workers to understand how to approach the emotional problems of these patients. I recognize that in tuberculosis as in all chronic diseases there may be neuroses, there may be psychoses, there may be psychosomatic conditions. There may be times when you must call the psychiatrist into consultation, but I believe his main job to be to teach the doctor

who is treating tuberculosis that, in addition to the pathologic aspect, there are sociologic and psychologic aspects, that there are problems in the family as well as in the patient, and that he must strive to understand the personality of the patient and handle him accordingly

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The contribution of psychiatry to the problem of tuberculosis is a chapter of psychosomatic medicine still to be written. There are two aspects to the problem—the question of etiology and the question of treatment. The emotional state of the patient can be considered in every disease as one of the etiologic factors, because chronic emotional stress has an influence upon all vegetative processes and does alter the resistance of the whole organism or of specific organs.

In the 19th century tuberculosis was the literary disease. The discovery of the bacillus of tuberculosis by Koch did not in the least invalidate the observation of earlier literary and medical men, that the outbreak of the disease often follows catastrophic events in the patient's life. Unfortunately, we do not know today much more than did these earlier observers about the specific nature of the traumatic emotional factors in tuberculosis.

Apart from precipitation of the disease, its course may be influenced by emotional factors. The resistance of the organism definitely depends upon the emotional state. Exactly how emotional processes increase or decrease the resistance of certain tissues we do not know. That is one of the most challenging problems for future research, and its solution may revolutionize therapy as much as have recent pharmacologic discoveries. Today our knowledge is merely empiric. We know that attention to the patient's emotional state is a prerequisite of sound medical care, and that this requires the technical knowledge of psychiatry cannot be contradicted. However, one may hope that with further progress in medical education, in the not too distant future every physician will have sufficient knowledge of the basic principles of psychiatry, so that he may include in his treatment considerations for the proper mental hygiene of his patients. Today the basic principles of bacteriology and physical hygiene belong to the conceptual armamentarium of every well-trained physician. He does not need to consult a bacteriologist to advise his patients in this respect. It can be hoped that in the not too distant future hospitals will use their psychiatrists only for treatment of special

cases, and will be able to entrust routine mental care of patients to the staff as a whole

Such every day, typical psychiatric problems as have been pointed out in this paper, the tendency for hospitalized patients suffering from chronic diseases to regress to a state of excessive dependency, manifesting itself in an irritating, demanding attitude, will have to become for every physician a matter of routine, just as are today bedsores or other common somatic sequelae of prolonged bed rest. The program of the National Jewish Hospital at Denver certainly is setting an exemplary standard for others to follow. In addition to the reform of undergraduate training, this type of consultation and teaching programs in hospitals can become important factors toward consolidating the new psychosomatic orientation which characterizes our present medical development.

### RESUMEN

Queríamos recalcar que todos los aspectos del servicio psiquiátrico que hemos bosquejado en este artículo son importantes y deben ser integrados efectivamente en el desarrollo de un adecuado programa de psiquiatría en el hospital para tuberculosos. Por ejemplo, nos parecería ser una empresa desesperada el intentar llevar a cabo un programa de enseñanza limitado en los aspectos psiquiátricos de la tuberculosis y esperar que podría ser aplicado sin la continua participación de un psiquiatrista y de un auxiliador social con orientación psiquiátrica.

Por consiguiente, recalcamos la necesidad de continuar el programa que hemos bosquejado y de orientar tal programa a base del concepto de participación psiquiátrica.

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# Thoraco-Hepatic Amebiasis\*

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JAMES P CONWAY, M.D and MISCHA J LUSTOK, M.D, F C C P  
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World War II has created and brought into closer focus many, heretofore remote, clinical problems One of these is amebic infection

The mass concentration of military personnel into areas endemic to amebiasis and the exposure of the soldier to a terrain devoid of sanitary control prior to his arrival, contributed appreciably to the epidemiology of this disease Sanitary regulations, especially if made purposely severe to compensate for lack of sanitary installations, are often disregarded under stress of combat areas

It is documentary knowledge<sup>1</sup> that one regiment, (under observation of J.P.C.), left an endemic area with a carrier rate of 23.4 per cent—as determined by rectal swab and normal stool examinations If fresh warm stools passed after a saline purge were examined, no doubt the percentage would have been even higher This figure is unusually high for Americans, and cannot be construed as an index of the carrier rate of all returned servicemen, but should focus the attention of the physician to a plausible etiology for the vague gastro-intestinal and pulmonary complaints of many veterans who have served in the Pacific Theater Service in the tropics is not, however, an essential prerequisite for such a diagnosis, for similar opportunities for amebic infestation existed within the endemic areas of the Zone of the Interior

We were interested in a group of patients with amebic infestation whose major presenting symptoms were of a pulmonary nature and whose early presenting signs were conspicuous in the thorax History of diarrhea was lacking or of mild nature Little significance had been attributed to it by the patient or the physician Frequently the patient was seen by the chest consultant first, because of the emphasis placed on the thoracic signs and symptoms Only after intensive etiological study at first, and more readily after experience matured, was the true secondary nature of the chest lesions fully appreciated and proper definitive

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\*From the Medical and Surgical Services Veterans Administration Hospital Wood, Wisconsin, and Marquette University School of Medicine Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinion expressed or conclusions drawn by the authors



management instituted. Classical signs of amebic infestation or typical medical history often were absent or vague in our cases. The type of patient who presents an adequate history, would have been screened and definitely managed in his earlier contacts with physicians.

The recovery of the parasite from the stool or tissue studies is the ideal criterion for diagnosis. This is difficult in some cases. In our experience, the presence of acute or recurrent right lower chest findings (effusion, pneumonitis, lung abscess) in an individual who lived in endemic areas, especially if associated with evidence of chronic hepatic involvement, has been adequate presumptive evidence for the clinical diagnosis of thoraco-hepatic amebiasis and indication for proper therapeutic procedures.

### *Case Reports*

During 1946, we had the opportunity to observe and treat ten patients with thoraco-hepatic amebiasis. Two patients had uncomplicated hepatitis, two had hepatic abscesses, one of which ruptured into the abdominal cavity, in three, a hepatic abscess had ruptured into the pleural cavity, one of which had also ruptured into the abdominal cavity, and in three, the hepatic abscess had entered the pulmonary parenchyma. Six had served in the Armed Forces in the Southwest Pacific, one in the India-Burma Theater, and three had never left the continental United States.

It is interesting to note that only four of these ten patients



FIGURE 1

*Fig 1, Case 1 Intra-hepatic density of liver abscess*

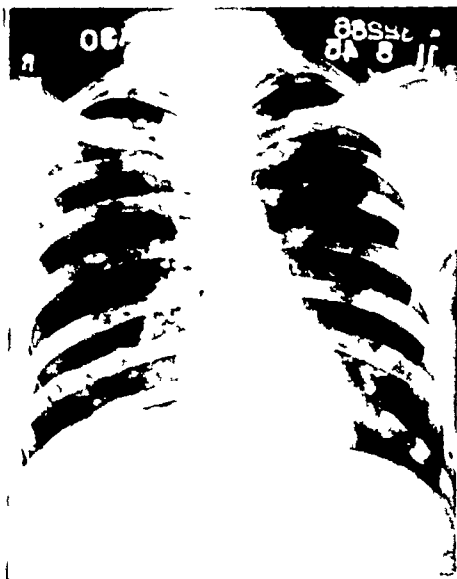


FIGURE 2

*Fig 2, Case 1 No significant chest involvement*

gave a history of diarrhea, and then not as a major event. Eight presented pulmonary and thoracic signs and symptoms of primary significance. Cysts of *E. histolytica* were recovered on stool examination in only four of this group. A direct smear from the wall of a liver abscess in one of the patients at postmortem examination contained the amebic trophozoite.

**Case 1** N A, 35 year old male, Army veteran, served in the Southwest Pacific in 1943 where he contracted malaria. He had six to nine recurrences. He was treated for malaria for two weeks prior to admission because of chills, fever and headache. Soreness in the epigastrium and bilateral costal margins and later vomiting appeared. A weight loss of 38 pounds was reported. No past history of diarrhea or dysentery was elicited. On admission, October 13, 1945, he appeared chronically ill. He was jaundiced and was tender in the epigastrium. He developed pain and tenderness in the right upper quadrant which spread to right lower chest. The liver became enlarged and tender. He ran an irregular, intermittent fever. A laparotomy done on November 10, 1945 revealed an abscess, 12 x 17 cm in diameter in the upper posterior portion of the liver. There was a smaller one on the inferior surface. They contained thick, chocolate-colored pus. The abscesses were incised and drained and the patient was placed on emetine therapy postoperatively. The abdominal operative wound drained profusely. After showing some improvement, he ran a septic downward course and expired December 27, 1945. Necropsy confirmed the postoperative diagnosis by demonstration of *E. histolytica* on direct smear from the wall of the liver abscess (Figs 1 and 2).

**Case 2** E S, 22 year old male, Army veteran, who served for approximately one year on Luzon and New Guinea in 1944-45, was admitted to

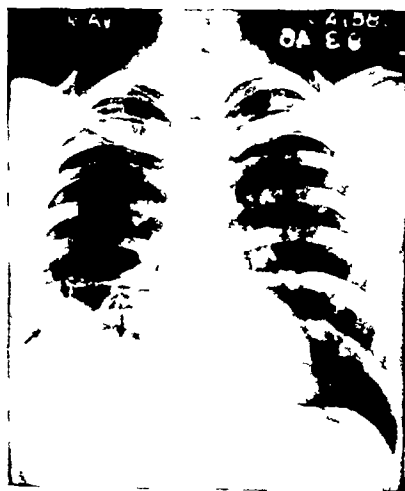


FIGURE 3



FIGURE 4

*Fig 3 Case 2* Extension of hepatic amebic abscess into pulmonary parenchyma—*Fig 4 Case 2* Fibrotic residuals after spontaneous bronchial evacuation of lung abscess

the hospital August 21, 1946, complaining of diarrhea of six month's duration. He had six to ten bowel movements daily containing blood and mucus. He had no diarrhea or dysentery overseas. Three weeks prior to hospitalization, he noticed the onset of aching pain in the right lower chest and right upper abdominal quadrant. At the same time, he developed a cough and pain in the right shoulder. Increasing weakness and exertional dyspnea occurred. Physical examination showed a pale, asthenic, chronically-ill white male who had a fever of 102 degrees F. There was limitation of expansion of the right chest with diminished breath sounds and tactile fremitus, as well as an impaired percussion note in the right lower lung field. There was tenderness in the epigastrium. Stools were positive for trophozoites of *E. histolytica*. He began expectorating chocolate-colored pus on August 26. The diarrhea subsided completely and his temperature came down to normal after a course of emetine therapy followed by carbarsone. Proctoscopic examination on August 29 showed small pin-point bleeding ulcerations suggestive of amebic colitis. A course of emetine and carbarsone was repeated beginning on October 14. Sixty cubic centimeters of chocolate-colored fluid were aspirated from right chest on October 18. No organisms or parasites were demonstrable in the fluid. The patient was clinically well by November 9, 1946. Surgery was held in abeyance because of excellent clinical response to medical management (Figs 3 and 4).

*Case 3* A B, 27 year old male, Army veteran, entered the hospital on July 15, 1946. He had diarrhea in the Philippines and Okinawa in 1945. An initial diagnosis of amebic dysentery was made at Oakland Regional Hospital. While there in January 1946, the patient began coughing up foul-smelling sputum which tasted like "pine-cone seeds." Following a course of emetine, he recovered and was discharged as well in March

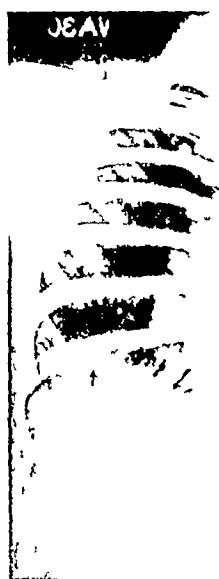


FIGURE 5



FIGURE 6

*Fig 5, Case 3* Rupture of hepatic abscess into lung parenchyma—*Fig 6, Case 3* Spontaneous evacuation of lung abscess with residual air seen under right diaphragm. This was evidence of broncho-hepatic fistula and indicated surgical intervention.

1946 When hospitalized here for a routine check-up on August 6, 1946, he developed a temperature of 103 degrees F, with recurrence of blood-tinged sputum which tasted like "pine-cone seeds" He improved with emetine therapy (Repeated stool examinations for *E histolytica* were negative) A third recurrence of rupture of the amebic liver abscess through the right diaphragm into the right lung on September 17 indicated surgical interference, and on September 27, a thoracotomy with decortication of the right lung was done Following removal of all drains, his postoperative course was uneventful He was discharged November 16, 1946, clinically well He returned on February 10, 1947 for follow-up study and was found to be in good health (Figs 5 and 6)

*Case 4* B S, 38 year old male, Air Force veteran, entered the hospital August 22, 1946 complaining of generalized chest pains, dyspnea and fever with expectoration of bloody sputum He had a similar occurrence in June 1946, for which he received penicillin, and salicylates without response A weight loss of 15 pounds during the past few months was reported No previous history of diarrhea or dysentery was elicited All his military service was in the continental United States, but he had come in contact with servicemen from the Philippines who had had amebic dysentery, and had used a common swimming pool Physical examination showed him to be acutely ill, temperature 101 degrees F, with physical signs of fluid in the right chest A roentgenogram of chest taken before admission revealed suspicious liver abscess with extension into the right lung On August 23, 500 cc of serosanguinous fluid were aspirated from the right chest and on August 28, cysts of *E histolytica* were found in his stools The patient was placed on a course of emetine and diodoquin An exploratory thoracotomy with decortication and drainage of abscess was done on September 13 His postoperative course was uneventful with subsequent complete clinical recovery (Figs 7, 8 and 9)



FIGURE 7



FIGURE 8

*Fig 7 Case 4* Liver abscess with linear pulmonary atelectasis above elevated diaphragm—*Fig 8 Case 4* Rupture of liver abscess into thoracic cavity

*Case 5* E R, was a 24 year old male, Navy veteran, who had served only in continental United States, but came in contact with servicemen who had had amebic dysentery and had used a common swimming pool. He was admitted to the hospital on May 1, 1946, complaining of pain in right chest and cough of three week's duration. The chest examination revealed distant breath sounds and a flat percussion note with crackling rales over right lower and posterior chest. A roentgenogram of the chest revealed a massive effusion in the entire right hemithorax. Aspiration of the fluid revealed a thick, green pus. The underlying lung which became visible after removal of the purulent fluid was suspected of having an intrinsic hepato-pulmonary lesion. All laboratory examinations, including numerous stool examinations, were normal. On May 25, a rib resection with drainage of an empyema cavity 10 cm in diameter in the right chest was accomplished. A right thoracotomy on July 22 revealed the presence of a subdiaphragmatic abscess which was incised and drained. It contained thick, grayish pus. A revision and broader resection with drainage of the empyema and subdiaphragmatic abscess involving the liver completed the surgery on August 8. Proctoscopic examination was negative. Remittent fever persisted until the patient received a therapeutic course of emetine followed by diodoquin. After several plastic revisions of persistent sinus tracts, complete clinical recovery followed (Figs 10 and 11).

*Case 6* A M, age 48, was a male veteran of World War I, who served in France in 1918. He had lived in Ohio and Wisconsin all his life. There was no past history of diarrhea or dysentery. He became sick with nausea, pain in the right hypochondrium and fever in July 1944. A laparotomy was done at Veterans Administration Hospital, Brecksville, Ohio, for the treatment of an amebic liver abscess. Drainage was instituted and ultimate recovery of patient resulted. On routine checkup, *E. histolytica* were found in his stools in January 1945. The patient com-



FIGURE 9



FIGURE 10

*Fig 9, Case 4* Early residuals after surgical drainage of liver abscess and overlying secondary empyema—*Fig 10, Case 5* Elevated diaphragm and overlying encapsulated empyema visible after aspiration of massive right pyothorax.

plained of soreness in the right lower chest and roentgenograms showed elevation of the right hemidiaphragm at that time. His symptoms subsided following a course of emetine. He was admitted to Wood Veterans Hospital on June 17, 1946, complaining of pain in the right lower chest, cough and fever of two week's duration. His stools were positive for cysts of *E. histolytica*. The patient left against medical advice (Fig 12).

**Case 7** W J, 26 year old male veteran, entered the hospital on May 9, 1946, complaining of pain in the right lower anterior chest of ten days' duration. The pain became gradually worse and was accompanied by vomiting. A weight loss of 24 pounds in the past six months was reported. He had had amebic dysentery on Leyte in January 1945, which responded to emetine. There have been three recurrences of pain in the right lower chest since that time. No diarrhea was noted with the last two episodes. He showed a respiratory lag, diminished tactile and vocal fremitus, impaired percussion note and diminished breath sounds in the right lower chest. Rigidity and tenderness in the right upper abdominal quadrant was noted. His temperature was 103 degrees F. The stools were negative. His temperature dropped to normal within three days after institution of emetine therapy. He became asymptomatic and the chest findings gradually returned to normal. Surgical intervention was not deemed necessary. Follow-up studies revealed no recurrence of chest disease. This case illustrates probable diagnosis of amebic hepatitis or very early amebic liver abscess with contiguous pleural reaction and effusion (Fig 13).

**Case 8** A R, a 39 year old male veteran entered the hospital on November 13, 1946, complaining of constant pain in the right upper abdominal quadrant for nine days. Fever, nausea, anorexia and weight loss were noted but no diarrhea was present. He had had diarrhea of seven days' duration while in India in 1944. The physical examination revealed



FIGURE 11



FIGURE 12

*Fig 11* Case 5 Iodized oil visualization of communication between residual empyema cavity and hepatic abscess after surgical drainage—*Fig 12* Case 6 Elevation of right hemidiaphragm with suggestive pointing of a recurrent liver abscess

a pleural friction rub with diminished breath sounds in the right lower chest. The liver was slightly enlarged and tender. His stools were negative for cysts and trophozoites. The complement fixation test was positive for amebiasis. A therapeutic course of emetine produced complete relief of symptoms and disappearance of physical signs within three days. Therefore, the diagnosis of thoraco-hepatic amebiasis was considered tenable (Fig 14).

*Case 9* R C, 28 year old male veteran, was admitted to the hospital on July 17, 1946. He had had intermittent diarrhea which started in the Southwest Pacific in 1943. A previous diagnosis of liver abscess had been made in January 1946. He had a temperature of 101.8 degrees F, an enlarged, tender liver and negative chest findings. The proctoscopic examination showed a healed cicatrix on the posterior wall of the sigmoid, interpreted as a healed amebic ulcer. His stools were negative for *E. histolytica*. A therapeutic trial with emetine produced complete clinical recovery within four days, suggesting the diagnosis of amebiasis.

*Case 10* J A B, 29 year old male veteran, entered the hospital on January 29, 1946, complaining of fever, weight loss of 30 pounds, pain in the right chest, right upper abdominal quadrant, and malaise. He had been sick for four weeks. There was no history of diarrhea or dysentery. He served in the Southwest Pacific and the Philippine Islands from 1944 to 1945. His temperature on admission was 101.2 degrees F. Tenderness in right upper quadrant, and right pleural effusion were noted on February 14. Eight hundred cc of lemon-colored fluid were aspirated from the right chest on February 26. The following day he experienced severe abdominal pain and generalized abdominal tenderness. Emetine hydrochloride therapy was started on February 28 and a laparotomy was performed. Generalized peritonitis, a subdiaphragmatic abscess and a liver abscess were found. The abscesses were drained. Postoperatively a

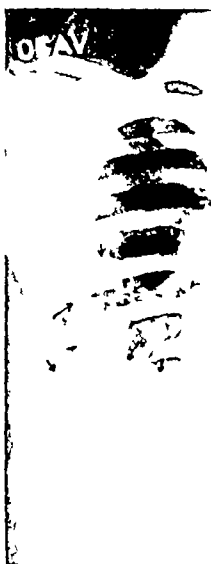


FIGURE 13



FIGURE 14

*Fig 13, Case 7* Elevation of right hemidiaphragm with contiguous pulmonary involvement—*Fig 14, Case 8* Moderate elevation of right hemidiaphragm with contiguous pulmonary involvement

course of emetine was completed and therapy continued with vioform, blood transfusions and daily irrigations of the operative wound. Following surgery, his temperature gradually fell to normal within two weeks. Intermittent fever recurred in May. It subsided after the administration of a second course of emetine and remained within normal limits the remainder of his stay. The anemia was improved by blood transfusions and iron therapy. Two additional chest taps for removal of fluid were necessary. Laboratory studies of the stools, and pus from the chest and abscess were all negative. The patient was discharged on June 18, 1946 as clinically well.

The most important extra-intestinal sites of amebiasis are the liver, lung and brain. The complications occur most frequently in the order listed.<sup>2</sup> Liver abscess is said to occur in about 20 per cent of the cases of amebic dysentery.<sup>3</sup> Approximately 35 per cent of the fatal cases have hepatic amebiasis.<sup>2,4</sup> Pleuro-pulmonary complications occur in about 15 per cent of patients having amebic hepatitis or abscess.<sup>5</sup>

The posterior-superior part of the right lobe of the liver is the favorite site for the amebic abscess in 70 per cent of the cases of hepatic amebiasis. It may rupture into the right pleural cavity, lung, or into the peritoneum. Another 15 per cent occur in the left lobe of the liver and may perforate into the left lung, pericardium, stomach or lesser sac of the peritoneum.<sup>6</sup> Pulmonary amebiasis may occur independently of hepatic abscess.<sup>7</sup> Whether primary or secondary, it closely simulates such pulmonary conditions as pleurisy with effusion, pneumonia, lung abscess, and tuberculosis. The rupture of a hepatic abscess into the lung may



FIGURE 15

FIGURE 16

Fig 15 Case 10 Elevated right hemidiaphragm without pleuro-pulmonary involvement—Fig 16 Case 10 Rupture of liver abscess into pleural space



sometimes be the first evidence of its existence<sup>7</sup> The mortality rate for the diagnosed abscess group ranges from 1 per cent<sup>8</sup> to 5 per cent<sup>9</sup> Prognosis is poor and mortality rate is high when multiple liver abscesses are present<sup>4</sup>

The diagnosis of thoraco-hepatic amebiasis usually rests on one or more of the following criteria (1) suspicious symptoms, physical findings and suggestive roentgenograms or fluoroscopy showing a domed elevation and fixation of the right hemidiaphragm with or without contiguous pleuro-pulmonary involvement, (2) typical proctoscopic findings, positive stools or positive sputum, and (3) therapeutic response to emetine

The treatment of amebic abscess of the liver is both medical and surgical in most instances Incomplete medical treatment alone results in too many relapses to be considered satisfactory All unruptured amebic liver abscesses should be aspirated if possible after the institution of emetine therapy, preferably after the fourth or fifth day This diminishes the possibility of seeding and removes the bulk of the involved material which presumably is one of the causes of relapses after medical therapy Open drainage of amebic abscess of the liver is seldom indicated unless there is a complicating pyogenic infection<sup>1</sup>

The treatment of complications of amebic abscess of the liver should be handled surgically with medical treatment maintained throughout the course of surgical management The more common complications is rupture of the abscess into the abdominal cavity or rupture through the diaphragm into the thoracic cavity Rupture into the abdominal cavity demands immediate surgical interference to provide drainage to the abscess bed

Rupture through the diaphragm into the thoracic cavity may be of two types

(a) Rupture into the free cavity which results in a very rapid total amebic empyema without appreciable involvement of the underlying lung This requires a wide thoracotomy through the bed of the 7th or 8th rib so that all the debris may be cleaned out of the thoracic cavity The hole through the diaphragm should be enlarged if necessary and abscess cavity wiped clean of debris The diaphragm should then be repaired and drainage to the abscess cavity provided subdiaphragmatically When the rupture has occurred more than four weeks prior to thoracotomy, decortication of the lung may be necessary This will be determined by the degree of expansion of the affected lung under positive pressure by the anesthetist Air tight intercostal underwater drainage or suction should be instituted postoperatively and continued as long as drainage occurs

(b) When rupture occurs through diaphragm in the absence of a free pleural space, erosion is likely to continue into the lung parenchyma and bronchus with a resultant broncho-hepatic fistula. History of the coughing up of chocolate material is obtained and roentgenologic examination reveals parenchymal involvement of the right lower lung, contiguous to a domed diaphragm.

Wide thoracotomy is advisable, as in the previous type, except that in addition, the diseased lung must be treated by segmental resection of the involved portions of the lower or middle lobes. Whenever possible, this should be done by beginning with the bronchial division and carrying the dissection distally from this point rather than attempting resection by clamping off what appears to be the involved segments. It is usually impossible to judge the actual involved area, and by using clamps one tends to either leave diseased bronchi and lung tissue or to cut across normal bronchi. When the involved lung has been resected, the opening in the diaphragm should be enlarged if necessary to clean out the liver abscess and repair the diaphragm over sub-diaphragmatic drainage. Since there is, as a rule, little appreciable pulmonary collapse from empyema in this type of rupture, decortication is rarely necessary.

### SUMMARY

1) Ten cases of thoraco-hepatic amebiasis are presented. Five of these cases were proven by isolation of the causative organism and the remainder were diagnosed on presumptive clinical and operative findings. Adequate clinical response to therapeutic management was observed in eight patients. In one instance, thoraco-hepatic amebiasis was not diagnosed until necropsy. One patient left against medical advice and could not be completely studied.

2) The most common locale for the original infestation with *E. Histolytica* was the Pacific area, however, three patients who never left the continental limits of the United States, were found to have systemic amebiasis. It is pointed out that each imported case of parasitic infestation may be a source for endemic spread of the disease.

3) The frequent absence of intestinal symptomatology in the clinical history, and the preponderance of chest symptoms with right upper abdominal pain, as the presenting major complaints, was striking. The observation of changes in the chest teleoroentgenograms was occasionally diagnostic, and as a rule, appreciably helpful in arriving at the proper clinical evaluation.

4) The medical and surgical management of thoraco-hepatic amebiasis as a complication of systemic infestation, is discussed.

## RESUMEN

1) Se presentan diez casos de amibiasis tóraco-hepática. Se comprobaron cinco de estos casos mediante el aislamiento del germen causante y los restantes fueron diagnosticados por los hallazgos clínicos y operatorios presuntivos. En ocho pacientes se observó una adecuada respuesta clínica al tratamiento. En un caso no se diagnosticó la amibiasis tóraco-hepática sino en la autopsia. Un paciente se salió sin permiso médico y no se le pudo estudiar completamente.

2) El lugar más común donde se originó la infestación con *E. histolytica* fue la zona del Pacífico. Empero, se descubrió amibiasis orgánica en tres pacientes que nunca habían salido de los límites continentales de los Estados Unidos. Se indica que cada caso de infestación parásita importada puede conducir a la extensión endémica de la enfermedad.

3) Fue sorprendente la frecuente ausencia de sintomatología intestinal en la historia clínica y la preponderancia de síntomas torácicos, y de dolor en la parte superior del abdomen, entre las principales quejas iniciales. Ocasionalmente la observación de alteraciones en los teleroentgenogramas torácicos estableció el diagnóstico y, por lo general, estas películas ayudaron a arribar al avalúo clínico apropiado.

4) Se discute el tratamiento médico y quirúrgico de la amibiasis tóraco-hepática como complicación de la infestación general.

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# Benign Pleural Effusion and Ascites Associated with Adenocarcinoma of the Body of the Pancreas\*

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In 1937, Dr Joseph V Meigs<sup>1</sup> of Massachusetts General Hospital brought to the attention of the medical profession the not infrequent occurrence of pleural effusion and ascites associated with benign ovarian tumors. Cases thought to be hopeless because of alleged pleural metastasis (postulated upon the finding of unilateral or bilateral pleural effusions) were cured by oophorectomy, after this surgical procedure the effusions were spontaneously and permanently absorbed. Meigs' syndrome has been reported in association with various sorts of ovarian tumors, including fibromata (the subject of Meigs' original report), cystadenoma, thecoma, granulosa cell tumor and Brenner tumor, as well as with uterine fibromata. About fifty cases of this syndrome have been reported to date. Two recent articles, containing reviews of the literature and bibliography, are those of Calmenon, Dockerty and Bianco<sup>2</sup> and Nora and Davison<sup>3</sup>.

I have been unable to find any reports of a similar syndrome in association with any tumors other than those of the female genitalia. The case which gave rise to the present report presents a similar syndrome in a male patient with a carcinoma of the body of the pancreas. This offers a challenge to the internist and the surgeon, since, just as in the case of Meigs' syndrome, the presence of recurring pleural effusions with ascites was considered evidence of hopeless metastasis.

*Case Report* The patient was a 58 year old man who entered Wood Veterans Hospital April 3, 1947. In the summer of July 1946 he had coronary thrombosis, necessitating two months of hospitalization. At this time mild diabetes mellitus was discovered, which was controlled by diet alone. The complaints upon his last admission were referred chiefly to the chest and consisted of dyspnea, chest pain, cough and expectoration. All had been present for ten weeks. Upon examination he appeared

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\*From the Medical Service, Veterans Administration Hospital, Wood, Wisconsin, Mark Garry, M.D., Chief of Service, with whose permission and cooperation this case is reported.  
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chronically ill and presented the findings of a bilateral pleural effusion. In addition, a rounded mass was discovered in the left upper quadrant of the abdomen. This was about 8 cm in diameter, firm and not tender, and moved slightly with respiration. Moderate hypertension was present. Laboratory tests revealed the following pertinent findings: Diabetic type of glucose tolerance curve, slight anemia, sedimentation rate of 11 mm, total plasma protein 6.6 gm per cent, plasma albumin 5.1 gm per cent, and an ECG showing myocardial damage on the basis of T-wave changes. There was x-ray evidence of a bilateral pleural effusion (Fig 1). In addition, x-ray findings were indicative of an extrinsic mass 8 cm in diameter displacing the stomach anteriorly and to the left. These findings were considered to indicate a carcinoma of the body of the pancreas with extensive pleural and peritoneal metastases. The clinical course was steadily downhill. The pleural effusions were aspirated repeatedly but recurred. The fluid was cloudy and amber. No tumor cells, tubercle bacilli, or other bacteria were found. About three weeks after admission, leg edema and marked ascites developed. A second total protein was 4.5 gm per cent with albumin of 2.7 gm per cent. After one of the numerous thoracenteses a traumatic left pneumothorax developed and despite repeated decompressions the patient presented progressive dyspnea and shock and expired on July 23, 1947.

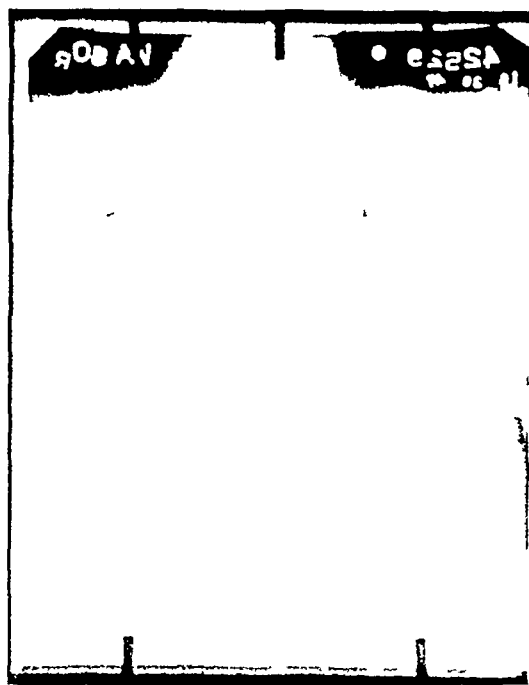


FIGURE 1

Autopsy (Dr A Swingle) The pertinent findings were as follows. The tumor was a cystic adenocarcinoma of the body of the pancreas. The only metastases were two minute nodules in the liver, measuring 1 and 4 cm respectively. Microscopically these were identical with the main tumor mass. The peritoneum was grossly normal and free of any metastatic deposits. Two thousand cc of reddish yellow fluid were present. The omental veins were markedly distended and tortuous as were the inferior mesenteric veins and other branches of the portal system. Both pleurae

were entirely free, grossly and microscopically, of any tumor tissue. Bilateral pleural effusion was found and in addition there was a tear in the collapsed left lung. The heart presented an old healed infarction in the lower portion of the left ventricle and the apex.

### *Discussion*

This patient had a large well encapsulated carcinoma of the body of the pancreas. Two small metastatic nodules were present in the liver. While the age of these nodules cannot be determined one may assume from their small size that they may have been of recent origin. It is not unreasonable to suppose that a tumor of this sort could have been extirpated in toto before metastases occurred. This is dependent upon ruling out distant metastases preoperatively. In the past, pleural effusion, in the presence of an abdominal tumor has been considered evidence of hopeless metastasis. May it not be that this situation will change in a manner similar to that now current in the field of gynecological surgery? Until Meigs clarified the benign nature of pleural effusion in the course of pelvic tumors a number of otherwise operable cases were denied surgery because of the presumably fatal significance of this finding. Perhaps the same benign evaluation may, at least occasionally, be given to the presence of pleural effusion accompanying other abdominal tumors.

The mechanism of the ascites in this case can probably be explained by the large tumor mass in the pancreas causing obstruction to the return venous circulation of the portal system. After the ascites developed, the low blood protein was a factor in the development of generalized edema. The extensive hydrothorax, recurring as it did, in the absence of any evidence of obstruction to the azygos vein or to the superior vena cava presented a much more difficult problem. In the numerous articles on Meigs' syndrome (for I assume the mechanism is probably similar in this case) several explanations are given. None of these explanations fits all of the facts nor satisfies the authors who propose them and I am unable to clarify that question here. Several cases have had the serum proteins studied, but as in this case, (upon the first examination) they were essentially normal. Air introduced into the pleural space or into the peritoneal cavity was not found to go through the diaphragm into the neighboring cavity.<sup>2,3</sup> India ink particles introduced into the abdomen have been found in the pleural fluid 48 hours later.<sup>2,3</sup> In several cases reported in the literature, examination of the two fluids has shown that they are apparently identical as to protein content and other chemical constituents. These last two observations seem to indicate that the two fluids are derived from a single source and it is believed that the ascitic fluid may reach the pleura

via diaphragmatic lymphatics The direct relation between the effusions and the pelvic tumors has been established by the fact that the fluid recurs after repeated aspirations but upon removal of the tumor the fluid is absorbed rapidly and permanently Perhaps some pathogenetic significance may lie in the fact that of the pleural effusions in Meigs' syndrome about 80 per cent are right-sided, about 10 per cent left sided, and the remainder bilateral

### SUMMARY

A case has been presented which was characterized by the presence of bilateral pleural effusion and ascites in the presence of an abdominal tumor At autopsy the tumor was found to be a pancreatic carcinoma with two small and probably recent metastases in the liver The effusions were found to be due to causes obscure in nature but not carcinomatous in origin It is suggested that this case may be analogous to cases of Meigs' syndrome, associated with a pancreatic tumor Every procedure should be exhausted to demonstrate the benign or malignant nature of the effusions in this type of syndrome If pleural metastases cannot be demonstrated and the abdominal tumor is amenable to surgery such surgery would then seem to be indicated

### RESUMEN

Se ha presentado un caso caracterizado por la presencia de derrame pleural bilateral, ascitis y tumor abdominal Durante la autopsia se descubrió que el tumor fue un carcinoma pancreático con dos pequeñas metastasis en el hígado, probablemente de origen reciente Se descubrió que los derrames se debieron a causas oscuras, pero no de origen carcinomatoso Se sugiere que este caso puede ser analogo a casos del síndrome de Meig asociados con un tumor pancreático Deben agotarse todos los procedimientos a fin de demostrar la naturaleza benigna o maligna de derrames en este tipo de síndrome Si no se pueden demostrar metástasis pleurales y el tumor abdominal es tratable por medios quirúrgicos, parecería que está indicada la operación

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# Tuberculosis and Carcinoma of the Lung

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The co-existence of pulmonary tuberculosis and bronchiogenic carcinoma was first reported by Bayle in 1810,<sup>1</sup> and by 1940 a total of only about sixty cases had been reported.<sup>2</sup> Reports have been more frequent in the past few years,<sup>3-5</sup> indicating either an actual increase in the co-existence of these two diseases or an increasing awareness of the existence of one disease in the presence of the other. However the diagnosis in most cases is still made at necropsy. It is the object of this paper to describe three more cases seen recently, principally to stimulate physicians to be alert to the possibility of the existence of carcinoma in cases of pulmonary tuberculosis which are behaving atypically.

*Case 1* The patient, a 52 year old white man, was admitted on June 16, 1942. His paternal grandfather died of carcinoma, four close relatives (two maternal uncles and two maternal aunts) died of pulmonary tuberculosis. He felt well until about two weeks before admission, when he suddenly developed cough, fever, chills, and pain in the right lower chest. From then on, he lost weight and became weak. Physical examination showed poor nourishment (height 70 inches, weight 120 lbs). Chest was symmetrical and expansion equal on both sides. Fremitus, resonance, breath sounds, spoken and whispered voice were normal, there were no rales, rhonchi, or friction rubs. X-ray film of the chest showed soft shadows in the right lung, from the first to the fourth interspaces anteriorly. Temperature was slightly elevated, never above 100 degrees F. Sputum was scanty and repeated concentration failed to reveal tubercle bacilli. Gastric lavage was performed on July 2, 1942, smear of gastric contents was negative, but on culture there was growth of typical colonies, and smear from the culture on July 31, 1942 revealed tubercle bacilli. Patient left the hospital against medical advice at this time. In August he noticed swelling of the neck, dyspnoea on slight exertion, and discoloration of the skin over the chest. Early in October he returned to the hospital. He was bronchoscoped and a biopsy specimen was taken, the laboratory report on tissue removed from the right main bronchus was "bronchiogenic carcinoma, squamous-cell type". In October, both arms began to swell and in November, both ankles began to swell. Examination by the thoracic surgeon at that time showed that the case was inoperable, patient was dyspnoeic and cyanotic at rest, veins of thorax, abdomen, and both arms were engorged, there was diffuse swelling of the tissues of the lower neck, there was considerable edema of the arms.

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(more on the right), and slight edema of the ankles, the pulse in the right arm was weaker than in the left, the axillary nodes were bilaterally enlarged, firm, and fixed, and the trachea was deviated to the left. Examination of the lungs revealed flatness, absent fremitus, and absent breath sounds on the right, and hyperresonance on the left. The abdomen was soft. The liver was palpable 3 cm below the right costal margin, and was nodular. Rectal examination was negative. Laboratory data: Stool examination was positive for occult blood, gastric contents showed no free hydrochloric acid, but did contain occult blood, gastrointestinal series showed deformity of the duodenal bulb, radiograph of the chest revealed the heart and mediastinal contents slightly displaced to the left, with a massive effusion on the right. Thoracentesis was performed on November 18 and 2,000 cc of fluid were aspirated from the right chest. Three deep x-ray treatments were given, but dyspnoea and cyanosis became progressively worse and the patient died on November 20, 1942. Necropsy was not performed. Clinical diagnoses:

- 1) Bronchiogenic carcinoma with extensive metastases to the mediastinum, liver, and axillary lymph nodes
- 2) Pulmonary tuberculosis

*Case 2* A 53 year old negro laborer was admitted on April 24, 1943, complaining of inspiratory pain in the right hemithorax, cough, expectoration, hemoptysis, and loss of weight and strength. Past and family history were negative. Examination showed an emaciated negro male lying quietly in bed, dyspnoeic and in pain. There was dullness to percussion, diminished but bronchial breath sounds and whispered pectoriloquy from the apex down to the third dorsal vertebra posteriorly and the fifth rib anteriorly, no rales, rhonchi, or friction rub. The heart was normal and in normal position, blood pressure was 112/72. The temperature was irregular, but rose as high as 102.6 degrees F. X-ray film showed homogeneous density filling nearly the entire right pleural space with the exception of small areas of aeration at apex and base. The urine was normal, blood count was normal, blood Wassermann was negative, and sputum concentrates were repeatedly negative for tubercle bacilli. On April 28, 1943 a needle was inserted into the right pleural space in the ninth interspace posteriorly, and 400 cc of thin but turbid yellow fluid aspirated. The fluid was negative on smear, but guinea pig inoculation revealed tubercle bacilli, as a result the diagnosis of pleurisy, serous, right, tuberculous, was made. Pain was constant and became increasingly severe. Dyspnoea became a prominent symptom. The patient assumed a peculiar posture, lying flat in bed, motionless, face downward, with rapid and shallow respiration. The right hemithorax became definitely larger than the left, but moved very little on respiration. Repeated attempts to aspirate fluid from the right hemithorax failed. X-ray film of the chest taken May 25, 1943 showed the entire mediastinal contents displaced to the left, the interspaces widened on the right, and an extensive area of homogeneous density almost filling the right hemithorax. On May 26, 1943 a large gauge aspirating needle was inserted into the right lung high in the posterior axillary line and 4 cc of soft granular tissue was aspirated. Microscopic examination revealed bronchiogenic carcinoma. Patient refused further treatment and left the hospital on June 3, 1943, on July 1, 1943 he died at home. Diagnoses:

- 1) Carcinoma, bronchiogenic, right lung
- 2) Pleurisy, serous, tuberculous, right

*Case 3* Patient, a 59 year old white man, was admitted on March 4, 1947. Family and past history was irrelevant. In the year prior to admission he had become weak and had lost thirty pounds weight. In the three months prior to admission he had noticed vague soreness in the right chest, slight dyspnoea, and cough, the cough was at first non-productive, then productive of a small amount of serous sputum, and finally productive of about an ounce daily of mucopurulent sputum. Three days before admission he became hoarse. Physical examination showed a markedly emaciated white man (height 5 feet 11¾ inches, weight 130 lbs). Temperature was 101.4 degrees F, pulse 100, respirations 22. Blood pressure was 90/70. Resonance was impaired and fremitus decreased over the upper third of the left lung. On admission, x-ray film revealed atelectasis of the left upper lobe, the left diaphragm was elevated but moved on respiration, there was a mass 4cm in diameter in the left hilum. The left vocal cord was found to be paralyzed on mirror examination and this finding was confirmed by laryngoscopy. A provisional diagnosis of inoperable bronchiogenic carcinoma, with involvement of the left recurrent laryngeal nerve, was made on admission. Sputum was repeatedly positive for tubercle bacilli on direct smear. Bronchoscopy was attempted three times, but was unsuccessful each time, the patient was apprehensive and poorly relaxed, so that visualization of the bronchial tree was not possible. Serial x-ray films showed extension of the atelectasis and of the hilar mass. On April 30, 1947, the whole left lung was found to be obscured, with retraction of the heart and mediastinal contents to the left. Thoracocentesis showed hemorrhagic fluid. He became steadily more dyspnoeic in spite of repeated thoracocenteses, he became cyanotic and pain became severe, so that he required oxygen and morphine. He died on May 28, 1947. Necropsy was refused. Diagnoses

- 1) Carcinoma bronchiogenic, left lung (tentative)
- 2) Tuberculosis, pulmonary, chronic, active

### *Discussion*

Pulmonary tuberculosis is still a common disease, in spite of the progress which has been made toward its control in recent years, and is being recognized fairly frequently in people past middle age. Carcinoma of the lung has been diagnosed with increasing frequency in the past decade, both clinically and at post-mortem examination. It is therefore to be expected that the incidence of the combined diseases, tuberculosis and carcinoma of the lung, should be reported more and more often, and this has been the fact in the past few years. There is a possibility that advancing carcinoma may invade healed foci of tuberculosis in which virulent tubercle bacilli survive, in such cases the freed tubercle bacilli would be responsible for a positive sputum and might cause tuberculous disease of the lung. It is believed that this was the sequence of events in Case 3 in which both clinically and roentgenologically all the evidence pointed to bronchiogenic carcinoma from the beginning and the diagnosis of tuberculosis was entertained only after the discovery of tubercle bacilli in the

sputum Rousseau and Côté<sup>6</sup> believe that carcinoma may produce anergy to tuberculin, thus favoring exacerbation of an arrested tuberculosis. Theoretically there is another way in which carcinoma may favor the development of active tuberculosis, that is, by producing general debility. Matz<sup>7</sup> believes that pulmonary tuberculosis or any other chronic disease of the respiratory tract, causes irritation of the respiratory tract which in some cases results in proliferation of the bronchial mucosal cells and metaplasia. In most cases the coexistence of these two diseases is probably mere chance.

When carcinoma is present in a tuberculous patient, it is important to make the diagnosis early so that pneumonectomy can be done with some prospect of success. The diagnosis is more difficult than in a nontuberculous patient, because the symptoms produced by the carcinoma are explained in the mind of the physician as being due to tuberculosis. If the physician will bear in mind the possibility of carcinoma in such cases, the correct diagnosis will be made much more often. In spite of a proven diagnosis of tuberculosis, if the symptoms are out of proportion to the size of the lesion, if there is unexplained dyspnoea or pain, if there is a change in the character of the cough and expectoration, and above all if x-ray shows an area of atelectasis, cancer should be suspected. The suspicion of cancer should cause the physician to secure at once bronchoscopy, cell block of sputum and pleural fluid, and biopsy of possible metastatic nodes. In Case 1 carcinoma should have been suspected in August instead of October, energetic institution of diagnostic procedures at that time might have brought the patient to the surgeon while pneumonectomy was feasible, whereas three months later he was inoperable.

### SUMMARY

1) Three cases are reported of co-existing tuberculosis and carcinoma of the lung. All cases were diagnosed during life, all cases were diagnosed too late for surgery.

2) The diagnosis of carcinoma in the presence of pulmonary tuberculosis depends on the same studies as in the absence of tuberculosis—x-ray, bronchoscopy, cell-block of sputum and pleural fluid, biopsy of suspected metastatic nodes, and exploratory thoractomy. The history is of diminished value, because the symptoms may be caused by tuberculosis as well as by carcinoma.

3) Carcinoma should be suspected when symptoms are out of proportion to the size of the tuberculous lesion, when there is unexplained dyspnoea or pain, or when x-ray shows an area of atelectasis. The diagnosis of carcinoma in the presence of pul-

monary tuberculosis is usually made too late because it is not suspected

### RESUMEN

1) Se informa sobre tres casos de tuberculosis y carcinoma del pulmon coexistentes. Se diagnosticó a todos los casos durante la vida, pero demasiado tarde para la intervención quirúrgica.

2) El diagnóstico de carcinoma en la presencia de tuberculosis pulmonar depende de los mismos estudios que en la ausencia de tuberculosis, a saber, radiografía, broncoscopia, exámenes de células en el esputo y el derrame pleural, biopsia de ganglios metastásicos sospechados y toracotomía exploratoria. La historia tiene menos valor, porque los síntomas pueden ser causados por tuberculosis lo mismo que por carcinoma.

3) Se debe sospechar carcinoma cuando los síntomas están fuera de proporción al tamaño de la lesión tuberculosa, cuando existen disnea o dolor inexplicables o cuando la radiografía revela una zona de atelectasia. Generalmente se hace demasiado tarde el diagnóstico de carcinoma en la presencia de tuberculosis pulmonar porque no se le sospecha.

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# Idiopathic Spontaneous Hemopneumothorax\*

## An Evaluation of Its Treatment and Report of Three Cases

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Idiopathic spontaneous hemopneumothorax is recognized clinically when intrapleural hemorrhage occurs in association with a spontaneous pneumothorax in otherwise apparently healthy individuals and is unrelated to trauma, malignancy, therapeutic pneumothorax, tuberculosis or other demonstrable disease of the lungs. Its close relationship with spontaneous pneumothorax is emphasized by its occurrence in individuals who have previously sustained an idiopathic spontaneous pneumothorax.<sup>1</sup> More significantly than in simple spontaneous pneumothorax, however, spontaneous hemopneumothorax is a grave emergency which requires prompt treatment because of the added threat of exsanguination superimposed on the cardiorespiratory disturbance resulting from collapse of a lung. A case fatality rate of about 30 per cent, death usually occurring within the first 24 hours, as reported by Hartzell<sup>1</sup> in 1942, should be subject to reduction in the light of current concepts of treatment if courageously applied.

The incidence of this condition is considered rare. Hartzell<sup>1</sup> in 1942 was able to find only 44 cases recorded, including those reported in his paper. Subsequently reports of 11 cases have appeared.<sup>2-11</sup> This probably does not represent the true incidence. Hartzell<sup>1</sup> reported four cases, Waring<sup>9</sup> had seen two and Hopkins<sup>12</sup> treated three. Three cases are reported here, all of which were observed within less than six months. One of us has seen an additional case not included in this report and we have knowledge of at least five other unreported cases.<sup>13, 14</sup> It seems not unlikely that any physician may be called upon to recognize and treat this interesting condition. That life may depend on the physician's success is well shown by the case reported by Helwig and Schmidt<sup>2</sup> and by the first case reported here.

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The pathogenesis, pathology and a detailed description of the clinical characteristics of spontaneous hemopneumothorax will not be discussed here as they have been adequately presented previously<sup>1</sup> and are now less controversial than the treatment. For this report, it is accepted that the bleeding results from vascular damage, whether at the time of onset of a spontaneous pneumothorax or subsequently as collapse increases and adhesions are torn. It is of some significance to realize that the bleeding vessel may be in the parietal pleura where it is not subject to control as collapse of the lung increases. It is also accepted that the persistent fluid state of the blood has been demonstrated to result not from a theoretical anticoagulant effect of the pleura but rather from rapid defibrination by cardio-respiratory action, resulting in a deposition of fibrin on the pleural surfaces. This is to be reckoned with in treatment if bleeding has been extensive. Determination of clotting properties of the aspirated blood may be used to decide whether bleeding has stopped. If there is still active bleeding, it is likely that the blood will clot on removal, whereas if bleeding has ceased and all the blood has been defibrinated, no clot will form.

Principles of treatment may be established for hemopneumothorax but the treatment of individual cases will of necessity depend on the nature and severity of the clinical manifestations. Several interrelated conditions exist. Sudden collapse of a lung disturbs the pulmonary circulation and reduces the oxygen saturation of the blood. Elevated intrathoracic pressure interferes with venous blood flow to the heart resulting in reduced cardiac output. Hemorrhage into the pleural cavity increases the degree of collapse of the lung and at the same time reduces the blood volume and the oxygen-carrying capacity of the blood. This also contributes to loss of cardiac output and produces hypotension. The ill effects from hemorrhage and from tension pneumothorax augment each other so that compensatory mechanisms are impaired. If bleeding is severe, profound and irreversible shock may develop rapidly unless active treatment is instituted. Reliance on a high intrathoracic pressure and low systemic blood pressure to stop the bleeding as suggested by numerous writers<sup>1 4 6</sup> may result in further unjustified mortality.

Treatment as outlined by Waring<sup>9</sup> in 1945 is more rational than that recommended by earlier authors. Aspirations of air and blood should be performed early and often enough to avoid high intrapleural pressure with resultant circulatory and respiratory embarrassment and mediastinal displacement. Replacement of air for blood aspirated, at this stage at least, is irrational. Transfusions should be given to maintain adequate blood pressure and

hemoglobin levels. The use of blood aspirated from the chest for transfusion has not been advised. Waing<sup>9</sup> has argued against it, stating that hemolysis and possible infection of the blood present a danger. However, if use of this blood may be lifesaving while donors are being obtained, as in the first case reported below, it is amply justified. Oxygen may be given as necessary in the acute period and rest and sedation should be maintained. When uncontrolled hemorrhage persists, thoracotomy has been suggested,<sup>9</sup> although we find no case recorded in which this procedure has been necessary. During the early period after the onset of a hemopneumothorax, the greatest danger of such a program of active treatment is the risk of infection from multiple aspirations. This can be reduced by the use of antibiotic drugs and should not constitute a handicap if such treatment can significantly reduce the mortality.

Once the acute phase is over and bleeding has stopped, different considerations govern the therapy. Shock and sudden death are not a problem but the speed and extent of recovery are related to the therapeutic management. Anemia is still to be combatted especially if any operative procedure is required. Infection of the pleural space must be avoided, or treated if present. Early and complete reexpansion of the lung is the aim of treatment in this period. The success with which expansion is achieved depends first on the presence of infection and second on the extent of fibrin deposits on the pleura. It is well known that small sterile hemorrhages will absorb without any demonstrable residual pleuritis. Jennings<sup>3</sup> noted that this is less readily accomplished by an encapsulated interlobar collection of blood than by blood free in the pleural space. Early aspiration is probably more significant in obtaining reexpansion than is late removal of defibrinated blood. Replacement of air when blood is aspirated would be considered only if a high negative intrathoracic pressure resulted. Decortication of the lung may be required where earlier treatment has been inadequate as in the second case reported here. Finally, for the patient who has a dry residual pneumothorax with a lung that is expanding poorly, instruction by a skilled physiotherapist in unilateral breathing may be of value. Once reexpansion is complete, pleural symphysis is apparently obtained. At least there is no record of a recurrence of hemopneumothorax.

Many of the treatment principles presented as related to idiopathic spontaneous hemopneumothorax would apply similarly to other types of hemothorax and hemopneumothorax. The incidence of infection in traumatic hemothorax is greater and decortication is much more likely to be required. Spontaneous hemopneumothorax developing during the course of pneumothorax treatment

for tuberculosis raises problems in the maintenance of the collapse therapy which are not germane to this discussion

### CASE HISTORIES

*Case 1* A 41-year-old white male was admitted to the hospital on the evening of November 6, 1946 complaining of pain in the left chest and shortness of breath. On the previous evening while driving a bus, he experienced a sudden pain in the left chest which radiated to the left shoulder and was accompanied by some shortness of breath. This was not preceded or accompanied by sneezing, coughing or other unusual exertion. Later in the evening the pain became more severe and he was treated symptomatically at his home. The following day he was worse and entered the hospital about 3 00 p m, some 24 hours after onset of symptoms.

There was no history of tuberculosis or other pulmonary diseases in the family, nor were there any known contacts with tuberculosis. There was nothing of significance in the past medical history. A wife and one child were living and well. Some slight cough had been present for years, which he attributed to smoking.

Upon admission to the hospital he was obviously dyspneic, pale and in pain. He had had little or no rest since the onset of symptoms. The pain involved all of the left side of the chest, left shoulder and left side of the neck. There was some evidence of cyanosis. The mucosae were pale. There was fullness of the left hemithorax with widening of the inter-spaces and diminished expansion on this side. No cardiac pulsations were seen. The percussion note was hyperresonant over the left, except at the left base posteriorly, where resonance was impaired. Breath sounds were absent on the left and were exaggerated on the right side. No heart sounds were heard over the left. On percussion, cardiac dullness was found to be to the right of the sternum. Heart sounds, likewise, were found to the right of the sternum. The rhythm was regular. Rate was 128 per minute and sounds were of fair intensity. No murmurs were heard. The pulse was thready in character. Blood pressure 90/75. The abdomen was flat, tympanitic and no tenderness or masses were noted.

Urinalysis revealed no abnormalities. Examination of the blood gave the following result: hemoglobin, 70 per cent, red blood cells, 3,600,000, white blood cells, 26,100. Polymorphonuclears, 88 per cent, lymphocytes, 10 per cent and monocytes, 2 per cent. An x-ray film of the chest (Fig. 1) showed complete collapse of the left lung with some herniation to the right side, and with marked shifting of the heart, trachea and mediastinum to the right. The film was made with the patient in bed in a semi-recumbent position, and the haziness over the left base was thought to be fluid. An electrocardiogram showed only a sinus tachycardia and some diminution of the amplitude of T-Waves in Lead 1.

The patient was given meperidine (demerol, Winthrop) 50 milligrams for pain, with but little relief. His condition became rapidly worse and evidence of shock increased. The pain began to spread downward over the abdomen, and increased resistance was noted over the upper abdomen. About 7 00 p m, a left thoracentesis was done. After removal of approximately 350 cc of air, under increased pressure, blood appeared in the syringe. This confirmed the impression of hemopneumothorax. Aspiration was discontinued after the removal of approximately 20 cc of blood. This did not clot. For a short time following this the patient



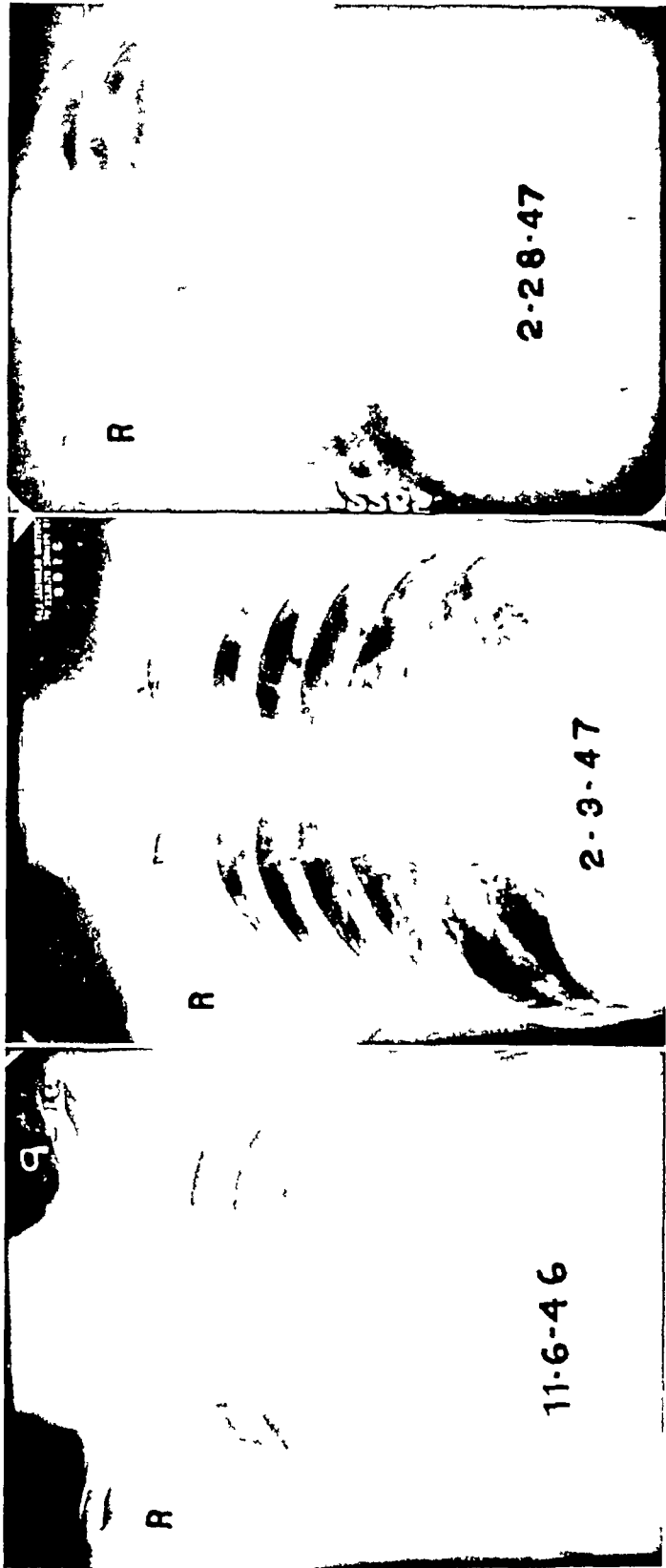


FIGURE 1

FIGURE 2

FIGURE 3

felt somewhat more comfortable, but by 9 00 p m he was again much worse and rapidly developed signs of collapse. He was seen by one of us about 10 00 p m. At this point he was in extremis and there was every indication that he would expire before anything could be accomplished. A needle was inserted into the left pleural cavity and an unmeasured quantity of air was removed, after which he promptly regained consciousness. Oxygen therapy was begun by nasal catheter and blood obtained for typing. It was apparent that he had lost a large portion of his circulating blood into the left pleural cavity. Since the need for transfusion of whole blood was emergent, and since some delay was inevitable in obtaining compatible whole blood, it was decided to transfuse him with his own blood removed from the pleural cavity. Accordingly, blood was withdrawn from the left pleural cavity into transfusion flasks and given intravenously.

During the night the left pleural cavity was aspirated many times, sometimes air was removed, sometimes blood. The removal of air was determined by the patient's symptoms. On two or three occasions he lost consciousness only to regain consciousness after removal of air. Frequent manometric readings were taken in order to keep the intrapleural pressure slightly positive. Altogether, approximately 1,800 cc of blood was removed from the pleural cavity and given intravenously. The amount of air removed was not measured. In the meantime donor blood was obtained and given.

By morning the patient's condition was still critical, though we felt that bleeding had decreased. Hemoglobin estimation at this time was 58 per cent and the red blood count was 2,800,000, in spite of almost continuous transfusion. Because of the possibility of contaminating the pleura by frequent taps, administration of penicillin was begun, 30,000 units intramuscularly, and was also introduced into the pleural cavity after aspiration. The patient improved during the day and by evening was definitely better. Aspirations of blood and of air were continued as indicated. The second morning bleeding apparently had stopped. Aspiration on two occasions yielded only 75 and 125 cc of blood. Pressure relations in the chest had become stabilized. The lung had begun to expand and the mediastinum and heart had begun to return to a normal position. The patient was much improved. Hemoglobin estimation at this time was 72 per cent, the red blood count was 3,400,000. Repeated sputum studies for acid-fast bacillus were negative.

From this point on, his course was that of gradual improvement. During the first few days his temperature varied irregularly between 99 and 102 degrees Fahrenheit. This returned to normal on the sixth hospital day and remained so except for occasional slight elevation. Penicillin intramuscularly was continued for several days after the temperature had returned to normal. He was then able to take a regular diet and his blood picture gradually returned to normal. Serial x-ray examinations of the chest showed gradual absorption of air and blood from the pleural cavity with return of the heart and mediastinum to normal position. He was discharged from the hospital three weeks after admission. At this time the lung had completely expanded. After a period of convalescence with slow return to activities, he was permitted to resume work three months after leaving the hospital, at which time there remained only some pleural shadows at the left base on chest films (Fig 2). He had gained weight and felt quite well.

*Comment* This case illustrates certain features which have been men-



FIGURE 6



FIGURE 5



FIGURE 4

tioned before The pneumothorax apparently occurred initially and was responsible for the sudden onset of symptoms There evidently was but little, if any, bleeding into the pleural cavity for several hours Upon admission to the hospital some 24 hours after onset of symptoms, there was blood in the pleural cavity and this accumulated rapidly during the next few hours That this condition can constitute a medical emergency, and that conditions can change rapidly are borne out Indications for prompt institution of therapeutic measures are well illustrated

Case 2 A 31-year-old white male was hospitalized February 25, 1947 He had served in the peace time army in 1939-1940 and had been discharged with a diagnosis of psychoneurosis, neurasthenia Between 1940 and 1946 he had complained of left chest pain and a complete study for chest disease was said to have been negative in January, 1946

On February 15, 1947, ten days prior to admission, while driving a car over a bumpy backwoods road he complained of severe pain in the left chest He continued to drive, but subsequently collapsed and was carried to his home After failure of the usual home remedies to relieve his "indigestion," a physician was called who told him that his heart was pushed to the right and that his left chest was full of fluid He remained in bed without specific treatment during which time he complained of dyspnea, weakness, and a feeling which he described as "fluid flopping about" in the left chest When he failed to improve, his doctor advised him to enter a hospital

On admission he was critically ill with marked anemia The red blood count was 1,600,000, the hemoglobin 30 per cent There was a massive effusion in the left chest, with displacement of the mediastinum, the heart lying in the right midclavicular line (Fig 3) Fever ranged from 102 to 105 degrees Fahrenheit the first few days, later dropping to around 100 degrees Oxygen, penicillin and sedatives were given During the first two weeks eleven thoracenteses were done with removal of 300 to 1,000 cc of bloody, foul-smelling fluid, the total amount removed exceeding 5,000 cc Six transfusions of 500 cc of blood were given Culture of the fluid was negative, as was the guinea pig inoculation for tubercle bacilli

On March 13, 1947 he was transferred to another hospital where he was seen by one of us On admission he complained only of left chest pain He was pale, thin, and appeared chronically ill The left chest was hyperresonant above the fourth rib posteriorly and dull below Breath sounds were absent throughout the left side and expansion of the left chest was markedly diminished Blood studies showed the red blood count 4,950,000, hemoglobin 83 per cent, white blood count 12,400 with normal differential count Serological examination was negative as were sputum and chest fluid studies for acid-fast bacillus and tuberculin tests with purified protein derivative Chest x-ray film (Fig 4) showed complete collapse of the left lung, density over the entire left chest, with multiple levels of fluid and air There was fever to 100 degrees Fahrenheit and some toxic manifestations with mental abnormalities of euphoria alternating with delusions of persecution which presented some difficulty of evaluation in view of a history of a previous suicidal attempt and other psychiatric abnormalities

On March 25, 1947 a decortication of the left lung was performed by Drs P D Elrod and J D Murphy through a parascapular incision with removal of a portion of the seventh rib The pleural space was found to be filled with a fibrinous jelly-like mass with loculated pockets of wine-



colored fluid This was removed leaving a fibroblastic membrane covering the entire pleural surface The lung was plastered against the mediastinum and pericardium With blunt and sharp dissection this was separated from the visceral pleura and the diaphragm The lung field was freed and its lobes separated With slight positive pressure the lung was reexpanded and successfully filled the entire thoracic cavity The chest cavity was closed and a catheter placed in the pleural cavity and connected to underwater drainage This was removed one week later

Pathologically the specimen removed consisted of two layers, one of fibrin and one of granulation tissue invaded by young capillaries

Postoperatively there was rapid reexpansion of the lung and clearing of the pleural densities Segmental breathing exercises were started one week postoperatively The patient was free of symptoms and up and around the ward on the tenth postoperative day A chest x-ray film on April 24, 1947 (Fig 5) revealed blunting of the left costophrenic angle and some thickening of the pleura at the apex of the lung The following day, one month postoperatively, he was discharged to his home

*Comment* This case appears to be the first reported instance of decortication for spontaneous hemopneumothorax A massive hemorrhage associated with infection with neglect during the first ten days resulted in a completely collapsed and functionless lung Aspiration was not successful and as a result of decortication five weeks after the initial bleeding, an excellent result was obtained Examination of the encapsulating membrane clearly demonstrated the futility of considering conservative treatment

*Case 3* A 19-year-old white male was hospitalized on March 24, 1947 His previous medical history had been negative except that in 1924 he was advised to discontinue saxophone playing because a routine x-ray film showed a "scab on the lung" Apparently no other significance was attached to this finding at that time He later served for 17 months in the navy and spent 14 months in the South Pacific area without illness

March 17, 1947 he had a slight hemoptysis described as one spot of blood not more than one centimeter in diameter On March 23 he awoke in the morning with pain in the epigastrium aggravated by coughing and deep breathing, with associated dyspnea Nausea and vomiting were induced by self-administered ingestion of strong salt water

When he was admitted on the next day to a hospital, x-ray film (Fig 6) revealed a tension hydropneumothorax with marked mediastinal shift, the right cardiac border being in the right anterior axillary line by physical examination Aspiration yielded bloody fluid This was repeated three times at twelve-hourly intervals with symptomatic improvement, however, the tension pneumothorax with marked mediastinal shift persisted through April 3, 1947 Thoracenteses with the removal of 100 to 300 cc of bloody fluid were repeated on April 4, 6, 8, and 21, but no attempt was made to remove all the blood, and a fluid level was allowed to remain above the level of the fifth posterior rib Temperature was 104.4 degrees Fahrenheit on April 4, 1947 and did not return near normal until April 26, 1947 He had received penicillin and sulfadiazine therapy The pleural fluid was sterile on three cultures On April 30, the red blood count was 3,620,000, hemoglobin 77 per cent and white blood count 8,300 with 65 per cent neutrophils and 35 per cent lymphocytes

May 1, 1947, 500 cc of bloody fluid was removed, May 5, 150 cc was aspirated and on each occasion 100,000 units of penicillin were instilled

and the pressure balanced. Further bleeding did not occur and the pneumothorax space remained dry. The fluid obtained was sterile. Chest x-ray film at this time (Fig 7) revealed an extensive adhesion binding the lung to the chest wall in the upper mid-zone laterally. Because of slow reexpansion of the lung, bronchoscopy was performed on June 4, 1947. No endobronchial disease was demonstrated but the lumen of the left bronchus was reduced in size, without secretion. Reexpansion of the lung remained slow, therefore he was referred to another hospital for consideration of decortication on June 20, 1947, at which time he was seen by one of us.

There was found to be a sixty per cent collapse of the left lung with multiple adhesions extending to the chest wall and demonstrable thickening of the pleura (Fig 8). Blood studies showed red blood count 4,990,000, hemoglobin 101 per cent, white blood count and differential count normal. The general condition was very good with a record of weight gain from 112 to 123 pounds during the previous six weeks. Decortication was considered but was not done because three months had lapsed since the onset, and organization and infiltration of the lung by the membrane was anticipated. In addition, slow but definite reexpansion had occurred between May 12 and June 20. Increased physical activity was encouraged and he was taught special unilateral breathing exercises under the supervision of the physiotherapist.

By August 12, 1947 virtually complete reexpansion had been obtained (Fig 9) and a well marked friction rub was present in the lower axilla. Diminished expansion of the left chest and reduction of the vital capacity to 85 per cent of the calculated normal revealed gross evidence of impaired function of the left lung nearly five months after the onset of the hemopneumothorax. He was discharged to his home on August 13, 1947.

*Comment* This is a case of a severe spontaneous hemopneumothorax with demonstrable adhesions put under tension by the collapse of the lung. This was presumably adequate to explain the bleeding. Early treatment was too conservative, as tension pneumothorax with mediastinal shift was allowed to persist for twelve days and aspirations were inadequate during the early treatment period so that a constricting pleuritis hampered reexpansion of the lung, with residual impairment of the respiratory capacity five months after the onset of the illness.

## SUMMARY

Idiopathic spontaneous hemopneumothorax is presented as a medical emergency with serious potentialities, which is somewhat more common than the infrequency of reported cases would seem to indicate. The principles of treatment have been presented, both during the early period when life is endangered from the combination of massive hemorrhage and tension pneumothorax, and during the late stage when reexpansion of the lung is the primary problem. The importance of active treatment with aspirations, transfusions, oxygen and sedation, with judicious use of thoracic surgery is stressed. Three cases illustrating important applications of these treatment principles are described in detail.

## RESUMEN

Se presenta el hemoneumotórax espontaneo idiopatico como una emergencia medica que acarrea potencialidades graves y que es algo mas comun de lo que pareceria indicarlo la rareza de los casos sobre los que se ha informado Se han presentado los principios terapéuticos, tanto durante el periodo temprano cuando la combinacion de hemorragia masiva y neumotórax hipertensivo amenazan la vida, como durante el periodo tardio cuando la reexpansion del pulmon es el problema primordial Se recalca la importancia del tratamiento activo con punciones evacuadoras, transfusiones, oxigeno y sedantes y el empleo sensato de la cirugia toracica Se describen en detalle tres casos que ejemplifican las importantes aplicaciones de estos principios terapéuticos

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# IX Congreso Panamericano del Niños

Caracas, Venezuela

## *First Section — Subject 3*

### PROPHYLAXIS OF INFANTILE TUBERCULOSIS

- 1) It was established that infantile tuberculosis must be maintained within the orbit of recognized fight against tuberculosis, such as the early discovery of the infectious cases and their segregation

To achieve the first a recommendation made a year ago by the XII Conferencia Sanitaria Panamericana was adopted as follows

It is recommended A systematic and periodic examination of masses of people apparently healthy, by method fluorophotographic introduced by De Abreu, and when the resources do not permit the general examination, preference should be given to those groups considered, under an epidemiological study, as more affected When this method is followed, also with the purpose of an epidemiological investigation, it must be complemented with tuberculin testing

The intensification of this procedure must not be done in detriment to the work of the Dispensary, which is the present base for the fight against tuberculosis

To enlarge the field of case finding activities, there must be promoted methods of teaching that will capacitate the general practitioner for the achievement of this purpose

To carry the segregation correctly, it is believed, that it is indispensable to allot for the fight against tuberculosis the necessary number of hospital beds according to the possibilities of each country, omitting other institutional types as preventoriums

- 2) It is believed that resistance to tuberculosis can be increased by indirect measures of non-specific nature or by direct ones of specific character

The first are all that tends to raise the standard of living, have the first consideration, emphasizing, when dealing with children on matters of education

The second, are represented until the present time by the BCG vaccination, the use of which is advised as part of the Sanitary Administration as an effective and already recognized prophylactic measure without interference with others

It is recommended the formation of an International Commission of Bacteriologists, physicians and statisticians to study means for standardization of production, make use and estimation of its value

- 3) It is recommended that greater attention be given than the one at present in some countries of the American Continent to the control and eradication of bovine tuberculosis

# Fifteenth Annual Meeting

## AMERICAN COLLEGE OF CHEST PHYSICIANS

Arrangements have been completed for the Fifteenth Annual Meeting of the American College of Chest Physicians to be held at the Ambassador Hotel, Atlantic City, New Jersey, June 2-5, 1949. Advance reservations for hotel accommodations indicate that the meeting will exceed all past attendance records. Every effort is being made by the Committee on Housing to accommodate members of the College who wish to attend the College meeting, as well as the Annual Meeting of the American Medical Association.

The Committee on Scientific Program has arranged excellent scientific sessions on all phases of diseases of the chest. Some of the features this year will be: Informal round table luncheon meetings, critical reviews of current developments in the specialty of diseases of the chest, a motion picture session, and an x-ray conference. There will also be luncheon meetings devoted to medical education, tuberculosis hospital standards and international affairs.

Oral and written examinations for Fellowship in the College and the following administrative sessions will be held at the Ambassador Hotel.

### THURSDAY, JUNE 2

- 8 00 a m Board of Examiners
- 9 00 a m Oral Examinations
- 2 00 p m Written Examinations  
Candidates are requested to report to the Board of Examiners at 8 30 a m
- 8 00 a m Executive Council and Committee on Certification
- 10 00 a m Annual Meeting, Board of Governors
- 12 00 noon Luncheon Meeting  
Annual Conference of College Chapter Officials
- 1 30 p m Committee on College By-Laws
- 2 00 p m Annual Meeting, Board of Regents
- 2 00 p m Council on Public Health,  
Committee on Chest Diseases in Penal and Mental Institutions  
Committee on Occupational Diseases of the Chest
- 2 00 p m Council on the Management of Diseases of the Chest,  
Committee on Surgical Treatment of Diseases of the Chest  
Committee on Non-Surgical Collapse Therapy  
Committee on Chemotherapy and Antibiotics
- 5 00 p m Council on Public Relations
- 7 00 p m Committee on Nominations
- 7 00 p m Council of Tuberculosis Committees
- 7 00 p m Council on Undergraduate Medical Education
- 8 00 p m Council on Postgraduate Medical Education
- 8 00 p m Council on International Affairs

SECOND ANNUAL POSTGRADUATE COURSE IN DISEASES OF THE CHEST, AMERICAN COLLEGE OF CHEST PHYSICIANS  
February 28 - March 4, 1949, Warwick Hotel, Philadelphia, Pennsylvania



Some of the physicians and instructors who participated in the Postgraduate Course in Diseases of the Chest held in Philadelphia

## FRIDAY, JUNE 3

- 8 00 a m Editorial Board  
4 00 p m Council of Tuberculosis Hospitals,  
Committee on Sanatorium Standards  
Committee on Rehabilitation  
5 00 p m Council on Research

## SATURDAY, JUNE 4

- 9 00 a m Administrative Session (Open to all members of the College),  
Report of the Historian  
Report of the Treasurer  
Report of the Executive Secretary  
Report of the Committee on Certification  
Election of Officers  
Reports of Councils and Committees

## SUNDAY, JUNE 5

- 5 00 p m Meeting, Board of Regents

The scientific sessions will begin on Friday morning, June 3rd at 9 00 a m, and continue through Saturday, June 4th and Sunday, June 5th

At 6 00 p m on Saturday, June 4th the College Convocation will be held. The Convocation will be followed by the Social Hour and Annual Presidents' Banquet

A convenient coupon for hotel reservations is published on page xiv of the advertising section in this issue

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## Second Annual Postgraduate Course in Diseases of the Chest Presented in Philadelphia

The Second Annual Postgraduate Course in Diseases of the Chest was presented at the Warwick Hotel, Philadelphia, under the sponsorship of the American College of Chest Physicians and the Laennec Society of Philadelphia, February 28-March 4, 1949. There were 44 physicians registered in the course representing 17 states, the District of Columbia, Canada, Argentina and Brazil

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## College Chapter News

### ARGENTINE CHAPTER

On December 11, 1948, the Argentine Chapter of the College held its annual meeting in Cordoba. An excellent scientific program on the use of streptomycin in the treatment of pulmonary tuberculosis was presented. The following members of the Chapter presented papers: Dr. Tomas de Villafañe Lastra, Dr. Rodolfo Cuchiani Acevado, Dr. Isaac A. Hassan, and Dr. Romulo Muzzio. After the scientific program the election of officers for 1949 took place. The new officers for the Argentina Chapter are:

Justo Lopez Bonilla, M.D., Rosario, President  
Oscar A. Vaccarezza, M.D., Buenos Aires, Vice-President  
Abraham F. Schottlender, M.D., Rosario, Secretary-Treasurer

### ARIZONA CHAPTER

The Arizona Chapter of the College will hold its annual meeting on May 10 in conjunction with the annual meeting of the Arizona State Medical Association, May 8-11, at Tucson. The following program will be presented:

"Pulmonary Resection in Tuberculosis—Indications and Results,"  
Reginald Smart, M D , F C C P , Los Angeles, California

"Mediastinal Tumors,"  
Thomas B. Wiper, M D , F C C P , San Francisco, California

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### CALIFORNIA CHAPTER

The annual meeting of the California Chapter of the College will be held at the Biltmore Hotel, Los Angeles, on Saturday, May 7, commencing at 2 00 p m. The following program will be presented:

"Pneumonia in Southern California,"  
Roger Egeberg, M D , Los Angeles

"Resistance Studies to Antibiotics in Tuberculosis,"  
Edward Dunner, M D , F C C P , Livermore

"Conservation on Chemotherapy in Tuberculosis,"  
Emil Bogen, M D , F C C P , Olive View

"Peripheral Vascular Disease in Chronically Ill Patients,"  
Elise Rose, M D , San Francisco

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### MICHIGAN CHAPTER

At the meeting of the Michigan Chapter of the College held on February 11th at the Detroit Tuberculosis Sanatorium the following officers were elected for the ensuing year:

William P. Chester, M D , Detroit, President

Cletus J. Gohnvaux, M D , Monroe, Vice-President

Constantine P. Mehas, M D , Pontiac, Secretary-Treasurer

Dr. Chester presented a talk on pneumoconiosis and several members recited their experiences with this disease.

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### MISSOURI CHAPTER

At the annual meeting of the Missouri Chapter of the College held in Kansas City on March 26th the following officers were elected:

Alfred Goldman, M D , St. Louis, President

Charles A. Brasher, M D , Mt. Vernon, Vice-President

A. J. Steiner, M D , St. Louis, Secretary-Treasurer

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### PORTUGUESE CHAPTER ORGANIZED

The organizational meeting of the Portuguese Chapter was held in Lisbon on March 28th. Professor Lopo de Carvalho, Governor of the College for Portugal, presided at the meeting.

## NEW YORK STATE CHAPTER

The New York State Chapter of the College will hold its annual meeting in Buffalo in conjunction with the annual meeting of the New York State Medical Society, May 5-6, 1949. The following program will be presented in the Section on Chest Diseases of the New York State Medical Society

"Mediastinal Emphysema with Spontaneous Pneumothorax,"

Donald R. McKay, M.D., F.C.C.P., Buffalo

Discussant David Ulmar, M.D., F.C.C.P., New York City

"Present Views on Streptomycin Therapy in Pulmonary Tuberculosis,"

William H. Stearns, M.D., New York City

Discussant Nicholas D. D'Esopo, M.D., Sunmount

"Experiences with Intracavity Drainage (Monaldi) in Pulmonary Tuberculosis,"

Warriner Woodruff, M.D., Saranac Lake

Discussant Allan Strahahan, M.D., Albany

"Exact Diagnosis of Pulmonary Tuberculosis,"

Herman E. Hilleboe, M.D., F.C.C.P., Albany

Discussant Nelson Strohm, M.D., F.C.C.P., Buffalo

"Diaphragmatic Hernia "

Herbert W. Meyer, M.D., New York City

Discussant John A. Stewart, M.D., Buffalo

"Bronchostenosis in Limited Pulmonary Tuberculosis,"

Edward N. Packard, M.D., Trudeau

Discussant George W. Wright, M.D., F.C.C.P., Trudeau

"Mediastinal Packing in the Treatment of Esophageal Varices,"

John Garlock, M.D., New York City

Discussant Max Som, M.D., New York City

"Decortication of the Lung in Non-Traumatic Lesions,"

Herbert C. Maier, M.D., and W. Fischer, M.D., New York City

Discussant Lew A. Hochberg, M.D., F.C.C.P., Brooklyn

Dr. Foster Murray, Brooklyn, and Dr. Samuel A. Thompson, New York City, are Chairman and Secretary, respectively, of the Section on Chest Diseases in the New York State Medical Society

## College News Notes

Dr. Angel Gines, Governor of the College for Paraguay, has been appointed Professor of Clinical Medicine in the Faculty of Medical Sciences, Asuncion

Dr. Edward P. Eglee, New York City, has been elected chairman of the executive committee of the New York Tuberculosis and Health Association

Professor Tefvik Saglam has been appointed Governor of the College for Turkey. Professor Saglam is also a member of the newly created Council on African and Near East Affairs of the College

At the annual meeting of the National Conference on Medical Service, held in Chicago, February 6, Dr. Walter E. Vest, Huntington, West Virginia, was elected a member of the executive committee. Dr. John S. Bouslog, Denver, Colorado, was named president of the Conference

## Obituary

EUSTACE THOMAS GOFF

1886-1948

Dr Eustace Thomas Goff, 62, of Parkersburg, West Virginia, died at his home in that city November 22, 1948, following a heart attack. Death was unexpected.

Dr Goff, whose specialty was diseases of the chest, was born at Hazel Green, West Virginia. He received his academic training at West Virginia University and graduated from the Medical College of Virginia in 1913. After engaging in practice at Smithville and Clarksburg, he moved to Parkersburg in 1922, where he remained in active practice until his death.

Dr Goff was a Fellow of the American College of Chest Physicians, a member of the Academy of Medicine of Parkersburg, the West Virginia State Medical Association, and the American Medical Association.

G. R. Maxwell, M.D., Governor for West Virginia

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## Book Review

INFANTILE TUBERCULOSIS, by Pierre Lowys. Preface by Professor Debie. Published by Flammarion, Paris, 1948.

The book presents a complete treatise on infantile tuberculosis, as useful to the practising physician to whom it brings everything he should know, as to the pediatrician or tuberculosis specialist, who will find in it the solution of all the questions bearing on the subject.

Having explained his modern conception of the evolution of tuberculous disease, and shown how the infant becomes tuberculous, Lowys discusses the clinical aspects, the development, the prognosis, the allergic manifestations, the tuberculin reactions and their variations, the laboratory data and their significance, illustrating the chapter on radiology by a number of plates. The differential diagnosis is presented from a specially critical and practical viewpoint.

The second half of the book is devoted to treatment (medical, collapse therapy, surgical, prophylactic). No detail is left uncovered. Based upon the observation of 2,000 infants, of 20,000 plates of the chest, at the sanatorium of Roddes-Fiz (Passy, Hte Savoie), arising from the particularly careful and benevolent experience of a pioneer in infantile tuberculosis as is Lowys, this book is an epoch making document.

Paul Veran, M.D., Nantes, France

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## AMERICAN ASSOCIATION OF RAILWAY SURGEONS

The Sixty-First Annual Meeting of the American Association of Railway Surgeons will be held at the Drake Hotel, Chicago, Illinois, on Thursday, June 30, Friday, July 1, and Saturday morning, July 2, 1949.

# DISEASES *of the* CHEST

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VOLUME XV

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## The Value of Streptomycin in the Treatment of Tuberculosis\*

HENRY C SWEANY, M.D., F.C.C.P.

Chicago, Illinois

It is with the greatest pleasure that I accept the invitation to deliver an address dedicated to the memory of Dr Carl A Hedbloom I do this with great humility and almost a feeling of inferiority We all recognized the worth of Dr Hedbloom while he was in our midst, yet as the years have passed his greatness has become even more magnified Without detracting from the merit of the fine young surgeons of the present time, I believe I may say that he stands alone among the chest surgeons of Chicago, having established in his specialty a tradition that will go down in medical history and will always be an inspiration for others to follow

Owing to the broad scope of the subject, the discussion of "The Value of Streptomycin in the Treatment of Tuberculosis" must be a general one, including references to the work already done as well as to our own incompleated studies Rarely has any medical problem expanded so rapidly, so extensively and so successfully Within a period of five years, Streptomycin has made more progress in the therapy of tuberculosis than all the other drugs of the past Before the advent of Streptomycin, hundreds of serums, vaccines and chemicals of all sorts had been tried with little or no success The results were generally so discouraging that there

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\*The Hedbloom Lecture, given February 16 1949, before the faculty and students of the University of Illinois College of Medicine under the auspices of Phi Beta Pi Medical Fraternity

From the Laboratories of the City of Chicago Municipal Tuberculosis Sanitarium

This investigation was supported (in part) by research grants from the Division of Research Grants and Fellowships of the National Institutes of Health, U S Public Health Service



was faint hope a therapeutic remedy would ever be found for tuberculosis

Domagk's<sup>1</sup> discovery of sulfa, however, opened a new line of search for chemotherapeutic remedies. Thousands of sulfa compounds were prepared not only for use against acute infections but for experimental study in the treatment of tuberculosis. Although a few sulfones were hailed with considerable enthusiasm, so far as tuberculosis was concerned little gain was achieved.

It was Fleming's<sup>2</sup> work on Penicillin, however, that began a new era in drug therapy and led to the present enviable position held by antibiotic therapy.

### *The Discovery of and Early Experiments with Streptomycin*

The discovery of Streptomycin was almost as phenomenal as that of Penicillin. Waksman<sup>3</sup> observed that practically no other micro-organisms were present in soil where certain *Streptomyces* existed. By growing some of these *Streptomyces* in media he was able to extract a substance that would suppress the growth of many bacteria. This product was called "Streptomycin," and Schatz, Bugie and Waksman<sup>4</sup> first showed the anti-bacterial effect of an extract of the *Streptomyces griseus* on bacterial cultures. Four grams of the "Streptomycin" were prepared for Feldman and Hinshaw<sup>5</sup> and later Feldman, Hinshaw and Mann<sup>6</sup> of the Mayo Clinic to try out on experimental tuberculosis in guinea pigs. The results were so encouraging that the immediate preparation of the product by the Merck Company was begun. As soon as the first product was ready it was tried out in pulmonary tuberculosis by Hinshaw and Feldman<sup>7</sup> and others at the Mayo Clinic.<sup>8, 14</sup>

Their work was a fair index of all that followed, and their conclusions were generally correct. They first showed that pulmonary tuberculosis could be considerably suppressed by the use of Streptomycin, that acute disease responded more readily than chronic disease, that cases of genito-urinary tuberculosis made a remarkable improvement after treatment with streptomycin, but that many relapses occurred. The drug was found to be useful in the treatment of tuberculous sinuses, tuberculous laryngitis and tuberculous tracheo-bronchitis, certain forms of military tuberculosis responded well. Even the dreaded tuberculous meningitis could be affected so that the lives of the patients were prolonged and some patients apparently cured of the disease.

It was soon obvious, however, that something was lacking, certain cases after a temporary improvement reversed their favorable course and became worse. As was soon discovered by Youmans, Williston, Feldman and Hinshaw<sup>15</sup> this was largely due to the

development of resistance to the drug by the tubercle bacillus. This resistance proved to be "the only discordant note in an otherwise perfect symphony."

The first experiments conducted at the Mayo Clinic created an air of expectancy in the medical world and caused those interested in tuberculosis to turn their attention to the use of this promising antibiotic.

*The Work in the Veterans' Administration,  
The Army and The Navy*

The Veterans' Administration, the Army and the Navy combined their efforts in one of the most elaborate experiments ever conducted in medicine. Protocols were laid down for the selection of cases, the time of treatment and the follow-up after completion of treatment. About two times each year a joint conference was held and all the data was assembled and discussed. Progress reports have appeared from time to time in medical journals.

Two of the first significant reports were published by McDermott, Munschenheim, Hadley, Bunn and Gorham<sup>16a</sup> and by Munschenheim, McDermott, Hadley, Hull-Smith and Tracy<sup>16b</sup>. These authors listed three cardinal features of the results of Streptomycin treatment, viz (a) a rapid, sometimes abrupt, fall in temperature and accompanying symptomatic improvement not unlike the crises observed in pneumococcus pneumonia, (b) a regression and frequently a complete disappearance of the pulmonary lesions demonstrable roentgenologically and (c) the development of strains of tubercle bacilli which were resistant to the action of streptomycin in vitro.

The earliest comprehensive report of the whole study appeared in December 1947, under the authorship of Barnwell, Bunn and Walker<sup>17</sup>. The criteria laid down for the selection of cases was rigid, namely there must be in each case selected a proved diagnosis, a minimal or moderately advanced exudative type of lesion or, if far-advanced, a prognosis of at least one year without Streptomycin. The patient must have been observed for 60 days and must not have shown any regressive changes during that period of time. Recent spreads or pneumonias were accepted. The same regimen was to be followed throughout the course of the drug treatment, for example a patient receiving pneumothorax was to be continued on pneumothorax as before, no surgical procedure was to be instituted during the course of the Streptomycin treatment, and an observation period of 120 days was outlined for each patient. The age limit for acceptable cases was 45 years.

Complete urine examinations were required three times before the beginning of treatment and every two days thereafter. Urea

clearance tests, non-protein nitrogen of the blood, sedimentation rates and sputum analyses were performed regularly X-ray films were taken before the treatment and every two weeks after the treatment was begun The pulse, temperature and weight were regularly recorded

The dosage selected was the same as that used in the latter part of the work at the Mayo Clinic, namely, 1.8 gms a day, given in six equally divided doses, for a period of 120 days The development of ear damage was controlled by caloric tests and audiograms before the treatment, at weekly intervals during treatment and at the end of the treatment

Analysis of these cases was carried on in a unique manner The President of the American Trudeau Society was called upon to appoint a jury of seven experts to read the roentgenograms The x-ray films were read individually by these men without any of them knowing whether a patient had or had not been treated, nor did any member of the jury know what the others had reported with regard to any film In spite of the fact that two-thirds of the lesions had showed progression before treatment was begun and that, according to the jury, 58 per cent would probably not have changed for the better if left on bed rest alone, 85 per cent of the "exudative" lung lesions showed some clearing

In general, the reduction of subjective clinical symptoms was quite dramatic Every patient on Streptomycin developed rather abruptly a feeling of well being The appetite improved in 85.2 per cent of the treated cases, weight increased in 84.3 per cent, cough decreased in 79.8 per cent, sputum decreased in 79.8 per cent, temperature decreased in 73.1 per cent, sedimentation rate decreased in 51.1 per cent, and sputum conversions were reported in 43 per cent during the treatment

The authors reported, however, that little or no substantial improvement occurred in the "proliferative" or "fibro-ulcerative" cases, since the treated and untreated groups remained about the same

It was noticed that there were certain signs of toxicity that could not be disregarded, especially the damage done to the eighth nerve There was a vertigo in 92 per cent of the patients treated and an absence or diminution of caloric stimulation in 77 per cent—indicating a definite injury to the labyrinthine branch of the eighth nerve There were many other minor variations from the normal nausea and vomiting in 10 per cent, elevation of temperature in 9 per cent, eosinophilia in 70 per cent, pruritis in 18 per cent, renal casts in 67 per cent, albumin in the urine in 20 per cent, and in 23 per cent treatment had to be discontinued because of urinary retention

The problem of resistance was studied by Youmans and his associates<sup>18</sup> who stated that 14 of 18 cultures (77 per cent) developed resistance in vitro Wolinsky, Renginster and Steenken<sup>19</sup> found resistance after twelve weeks treatment in 37 per cent of 47 cases

As a result of the difficulties encountered with drug toxicity, bacillary resistance and various other factors, a much wider scope of study was outlined by the above mentioned Government Services<sup>20</sup> Several different categories with regard to dosage and length of time of treatment were outlined and followed As a result of this second report, involving 2,780 cases, the authors were able to state among other things that in addition to the previous findings the one-gram dosage was as satisfactory as the two-gram and that probably even 0.5-gram sufficed One of the most important observations was that a remarkably small number of complications resulted from the half-gram dose given in two equal daily injections The one-gram dose produced less than half the number of complications resulting from the administration of the two-gram dose, the half-gram dose produced only a half to a quarter as many complications as the one-gram dose In fact, of 137 cases treated with the 0.5-gram dose there were no cases in which the caloric stimulation was entirely absent and none in which there was diminished hearing to voice sound, while only 5.8 per cent of the cases revealed vertigo, compared with 23.1 per cent of those on one-gram dosage and 80 per cent on the two-gram dosage

There was a clinical improvement in practically 75 per cent of all cases treated The jury (now of ten men) reported that only 9 to 13 per cent of the cases had improved before the drug was given and that 71 to 75 per cent showed improvement roentgenologically after the drug was given In spite of this favorable showing, the authors warned that every case of tuberculosis was not suitable for treatment and that very few cases cleared completely Most of the roentgenograms cleared only partially, relapses occurred in 7 to 10 per cent of cases during treatment and 14 to 29 per cent after treatment

Since that report, the time of treatment has been further reduced to 42 days in an attempt to avoid development of resistance of the bacillus

By this time they were also able to offer a more favorable appraisal of the treatment of certain complications The results of the work on bones and joints was particularly gratifying, 40 per cent of the cases improved during treatment and 70 per cent after the termination of treatment, whereas 70 per cent of cases were progressive when treatment was begun The treatment of

tuberculosis of the genito-urinary tract produced symptomatic improvement, cystoscopic improvement, and a conversion in bacillary content in 80 per cent of the cases treated, while only 15 per cent showed relapses. The only difference between this complication and some of the others was that better results were obtained on the two-gram than on the one-gram dosage. The most disappointing of all the complications treated were the miliary and meningeal lesions. While it was true that many cases made temporary recoveries and that something had been accomplished in the treatment of tuberculous meningitis that had never before been done, nevertheless, only a small percentage of the total number of cases treated ultimately survived. The work from the Service groups was reported recently by Bunn<sup>21</sup> who has followed the cases from the beginning of treatment. Out of 100 such cases only 24 were alive from 11 to 25 months after treatment, of this 24 only 15 were entirely well. A further break-down of the 24 living cases revealed that 12 were of the 22 miliary cases, 9 were of 43 simple meningitis cases and only 3 were of 35 cases of miliary meningitis cases.

Treatment of other complications produced results similar to those reported in the preliminary series. Included were gastrointestinal lesions, laryngeal lesions, lesions of the cutaneous sinuses, of the mouth, the pharynx, and of the tracheobronchial tree and many other complications where there were not a great many cases treated. For example, in tuberculous lymphadenitis, out of 36 cases there were 12 in which the lymph node enlargement had disappeared, in 18, nodes were much smaller and in only six were the findings stationary. There were good results in many cases of tuberculous peritonitis, 19 of 27 cases improved, with some showing complete recovery. In otitis media, 11 out of 13 cases improved and some were healed completely. Several cases of pericarditis were apparently healed. Particularly gratifying were the results from thoracic surgery, especially on pulmonary resection where there was a percentage of only 2.8 per cent post-operative spread, compared with a very much higher percentage before the use of Streptomycin. The results with other types of lung surgery were not especially remarkable.

The authors reiterated that there was little or no effect on chronic fibroid pulmonary tuberculosis. The effect on cavities was unpredictable and if any favorable action was present it was usually temporary. Because of the possibility of the development of resistance, it was recommended that Streptomycin treatment not be used in minimal cases of tuberculosis which could be well handled by other means.

An important observation was that collapse therapy was made

feasible in 20 per cent of their cases as the result of Streptomycin treatment. They recommended that collapse therapy be initiated before resistance of the micro-organism developed.

*The Work of the American Trudeau Society and the Tuberculosis Study Section of the U S Public Health Service*

Almost simultaneous with the program outlined and followed by the Service groups was the work of the American Trudeau Society\* in conjunction with the Tuberculosis Study Section of the United States Public Health Service\*\*. In fact, there was an over-lapping of the workers in these two groups, a great many in the Service groups were on the Committee of the United States Public Health Service Study Section. This Committee has met two or three times a year and passed upon appropriations for various hospitals and institutions outside of the Government Services. A large number of separate studies are being supervised by the Committee, which in addition has undertaken a vast experiment in which a large number of cases are being treated with matched controls. It is too early yet to expect an analysis or evaluation of the results of this interesting study.

Like the Service groups, and profiting by their experience, the United States Public Health Service Committee found it necessary to outline several categories for the study of the length of time and dosage. Dosage schedules were reduced from two-grams to a rough "gram per body weight" dosage of 0.75 to 1.5 grams, depending on the weight of the individual. Also, as in the Service groups, the time element was reduced from 120 to 90 and then to 60 days.

Some of these studies have already been published. A representative report is one by Amberson and Stearns<sup>22</sup> which has summarized the situation clearly with regards to indications, complications, dosage, time of treatment and results.

*Studies Abroad*

As soon as the drug was available, work was begun in many of the countries of Europe and Latin America. Some of the earliest and most important reports, largely concerned with the treatment of generalized tuberculosis, include those of Cocchi and Pasquinucci<sup>23</sup> in Italy, Debré,<sup>24</sup> Decourt,<sup>25</sup> DeLavergne,<sup>26</sup> and Bernard<sup>27</sup> and their respective associates in France, Van Goidsenhoven and his associates<sup>28</sup> in Belgium, Marshall<sup>29</sup> and his many associates in England and Löffler<sup>30</sup> and his many associates in Switzerland. A significant fact observed was that there was

\*Dr McCloud Riggins, President, succeeded by Dr H Corwin Hinshaw

\*\*Dr E R Long, General Chairman, and Dr H Stuart Willis, Chairman

immediate favorable clinical effect in the majority of all treated cases of generalized tuberculosis, resulting in a relief of symptoms and prolongation of life

They found recurrences of the disease in most of the treated cases, and that apparent recoveries varied from 50 per cent down to around 10 per cent of the cases. This variation depended on several factors, the most important of which was the length of time the cases were followed after treatment. Another important factor was the type of the disease, the mortality was highest in military meningitis, lower in simple meningitis and lowest in military tuberculosis. In addition, results were reported to be better in proportion to the shortness of the disease's duration before treatment. Finally, patients with meningitis fared better with intrathecal treatment, but it was necessary that the dosage be kept low (between 25 to 50 mgs) and given at the onset every two to three days and then at various longer intervals. Many of the authors claimed an advantage in the intrathecal use of various ancillary drugs (sulfones, vitamins, etc) with Streptomycin.

#### *The Streptomycin Work at the Municipal Tuberculosis Sanitarium*

About November 1946, the first cases were treated at the Municipal Tuberculosis Sanitarium. At first we were obliged to treat only those patients who were able to buy the drug themselves.

This situation proved to be most unsatisfactory since it resulted in the treatment of many unsuitable cases which not only were left unimproved but also were subject to the ear damage commonly resulting from the large dosage employed at that time. The two-gram dosage was soon supplanted by a modified dosage outlined by the Tuberculosis Study Section of the United States Public Health Service, with a marked reduction in ear complications. A Streptomycin Board\* was appointed to study each case carefully and make selections for treatment on the basis of indications already determined, to obtain the maximum results and to prevent drug toxicity as much as possible. About all that could be done under the existing conditions, however, was to watch for signs of toxicity and to classify the cases into those having good and poor indications, since anyone might buy his own drug.

In November 1947, the problem was greatly simplified when the Board of Directors\*\* of the Institution provided for the purchase of Streptomycin for all patients who might benefit from the use

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\*LeRoy Berard, G. W. Holmes, M. R. Lichtenstein, George C. Turner and Henry C. Sweany, Chairman

\*\*Dr. Ernest E. Irons, President, Dr. Herman N. Bundesen, Vice-President and Mr. Philip Weber, Secretary

of the drug and authorized the Streptomycin Board to select cases according to medical indications

Almost simultaneously it became evident that there were possibilities of still further reducing the dosage without a corresponding reduction of the drug's therapeutic effect. There were only two studies at the time on which we could base our judgment since the work of the Service groups and the United States Public Health Service was just getting under way. Karlson and Feldman<sup>31</sup> of the Mayo Clinic reported that in guinea pigs of 677-700 gms a dosage of six to eight mg was as effective as larger amounts. By analogy, a 50 kilogram person would do well on a dosage of 0.5 to 0.6 gram a day. Since results in animals should not be translated to humans directly we relied more on Bogen's work<sup>32</sup> on human beings, which demonstrated that 0.5 gram a day and even as little as 0.2 gram would heal tuberculous tracheobronchitis. Only on a dose as low as 0.1 gram did he notice any decrease of the drug's effect on the lesions. With these two studies before us we made the decision to adopt a 0.5 gram dose for all patients weighing less than 150 pounds and 0.75 gram for all patients over that weight, except in the cases of miliary, meningeal, genitourinary, bone, joint, lymph node and pericardial tuberculosis where 1 to 1.5 gram doses were continued. The value of this dosage has been substantiated by our work and by the work of the Service groups.<sup>20</sup>

The change in dosage had many desirable advantages. There has been to date only one case of serious labyrinth disease on the low dosage. In addition, the cost of the drug per patient was greatly reduced. There was less nursing care necessary since fewer daily doses were required.

Along with this reduction in dosage came the reduction in the length of time of treatment, first from 120 to 90 then to 60 and finally to 45 days. The Service Groups' minimum time was established at 42 days.

Justification for reducing the length of time of treatment was offered by Barnwell, Bunn and Walker<sup>20</sup> in human tuberculosis. These authors observed that maximum results were obtained rather early in the treatment and that prolonged treatment did not always benefit the patient. These same authors as well as Bernstein, D'Esopo and Steenken<sup>33</sup> indicated that the arrest of progress of the healing was partly due to resistance which was found to develop in as high as 80 per cent of the strains of bacilli during the second to the fourth month of treatment. Another important observation made by Feldman and his associates<sup>34</sup> and Steenken and his associates<sup>35</sup> was that tuberculosis produced in guinea pigs by resistant micro-organisms was not helped by



Streptomycin treatment The work was therefore becoming increasingly complex as time went on

The control work at our Institution was carried out along lines similar to those recommended by the Service groups and the United States Public Health Service Committee, with the exception that the laboratory and x-ray control work was usually not as closely spaced because of the lack of technical help

Except at the beginning only the more acute types of disease, those in which there were recent infiltrative processes with or without excavation, were considered for treatment

The obligatory haphazard method of case selection prevailing at the beginning of our work was not all in vain We found that little permanent gain accrued from treating certain types of the disease, notably advanced caseo-pneumonic and chronic fibroid types Although the work of Howlett and O'Connor<sup>36</sup> has shown that many temporary favorable clinical results may be obtained by the treatment of the chronic type of case, most of the improvement that they noticed was "not sufficiently consistent nor definite to justify wide use in the chronically active and unstable cases of pulmonary tuberculosis" Many fibroids with acute infiltrative lesions justify a short trial of the drug, especially if there is a chance for surgery Even a relatively recent cavity may be affected and partly closed by some as yet unexplained effect on the bronchus entering the cavity The treatment probably clears some of the inflammation around the valvular opening which automatically removes the tension, and if the wall is not too thick the cavity will collapse In the walls of recently formed cavities the bacilli may also be attacked by the drug In long standing chronic cases, however, especially those who are ambulant or might become ambulant without closing out the bacilli, treatment is definitely contra-indicated not only because of the ineffectual results but because of the danger of creating and disseminating resistant bacilli

Practically all the complications of the disease and the drug treatment itself have been handled as recommended by the earlier studies, with generally similar results We found contact dermatitis of the nurses a disturbing problem until protective measures were adapted

The following figures and comments represent an interim report of the over-all Streptomycin program at our Institution Final analysis will not be supplied at this time since practically all the specialties involved are to be included in more complete studies to be given later McEnery and his associates<sup>37</sup> have already reported on the treatment of progressive primary tuberculosis in children The reports on the treatment of orthopedic, proctologic,

laryngeal and enteric tuberculosis, on surgical tuberculosis and on the bacteriological studies are being prepared

There is an insufficient number of cases of the other complications to warrant special reports as yet. Accordingly the genito-urinary, lymph node, miliary, meningitic and other organ-localized tuberculosis, as well as tuberculous sinuses and fistulae, will be included in the complete report of which this paper is only a preliminary

In the whole series, the treated cases may be arranged into four main groups based on the degree of recovery. First, there are those which have shown no change, with the possible exception of an emperhermal improvement in subjective clinical symptoms which might even be ascribed to a psychic effect, second, those which have shown definite improvement in subjective symptoms for several days to a few weeks, but few or no other changes, third, those which have shown marked change in subjective clinical symptoms and in addition have shown clearing on the x-ray films and improvement of most laboratory tests, but only temporarily, and fourth, those which have shown considerable or marked changes of an apparently permanent nature

Up to the present, 1,012 patients have been treated, and in 863 the treatment has been completed. Of the latter, 470 (54.5 per cent) have shown a substantial and lasting improvement. Although a few cases of extra-pulmonary tuberculosis improved when the lung lesions failed to improve, the numbers were not enough to distort the main findings. In general, this group did not include most cases suitable for primary pneumothorax and thoracoplasty, although a small number of such operated cases have been treated with Streptomycin prophylactically.

Of 670 non-surgical cases 371 (comprising 55.4 per cent of the group and 43.0 per cent of all treated cases) have shown an unmistakable favorable response, many of these have been discharged or are in the process of being discharged.

Of 371 non-surgical cases responding favorably 223 (comprising 60.1 per cent of the group and 25.8 per cent of all completed treated cases) were pulmonary and 148 (39.9 per cent of the group and 17.2 per cent of all) were non-pulmonary cases. Practically all the cases classified as "non-pulmonary" had some pulmonary disease which responded with wide variation to the administration of the drug. A correct analysis of all aspects of these cases obviously must await the complete report.

Surgery was recommended in 193 cases (22.4 per cent of all treated cases), 99 (11.5 per cent of all cases) received surgery and 66 (7.7 per cent of all cases) were prepared for surgery but have not yet been operated on. Twenty-eight (3.2 per cent of all

cases) of those which received surgery developed some postoperative complication

Of the pulmonary cases treated, 178 were of the infiltrative or dense caseo-pneumonic types of which only 72 (40.5 per cent of the group and 8.4 per cent of all treated cases) had a more or less permanent favorable result. The poor showing of this group is due to the fact that many "palliative" cases and, particularly during the early stages of the work, cases with poor prognosis, were included. Of 202 progressive fibrocaceous and fibrocaceous and ulcerative types, 113 (55.9 per cent of the group and 13.1 per cent of all treated cases) showed a favorable result, 22 of 29 progressive primary lesions in children were permanently improved, 14 of 15 bilateral fibrocaceous and ulcerative cases with pneumoperitoneum were markedly improved, and two of seven cases of miliary tuberculosis were improved and are still living. The results on extra-pulmonary tuberculosis are shown in Table II.

The findings are what might be expected from the type of cases treated. For example, there were several seriously ill cases with far-advanced pulmonary disease in addition to the complication, who did not show anything more than temporary improvement of subjective clinical symptoms of the pulmonary process even if the complication improved. Those with broncho-pleural fistulae nearly all had cutaneous fistulae as well. Several of these combined fistulae have as yet failed to respond to treatment.

It should be pointed out also that the number shown in the table include only the cases primarily selected for the treatment of the complication irrespective of other disease present. For example, there were only six cases selected for treatment of ano-rectal tuberculosis, but there are 18 other cases having ano-rectal

TABLE I  
Pulmonary Tuberculosis (Non-Surgical) Treated With Streptomycin

TYPE OF DISEASE	— R E S U L T S —	
	Favorable	Temporary or No Improvement
1 Acute infiltrative or caseo-pneumonic	72 (42.8%)	96
2 Progressive lesions (fibrocaceous and/or ulcerative)	113 (55.9%)	89
3 Streptomycin with pneumoperitoneum	14 (93.3%)	1
4 Progressive primary in children	22 (71.0%)	9
5 Miliary	2 (22.2%)	7
TOTAL	223 (52.5%)	202
GRAND TOTAL		425

complications in cases treated for pulmonary disease, enteritis, etc. A complete presentation of every aspect of each case must wait the report of the various specialties and a complete analysis of all the data.

Without including the 66 cases who have not yet received surgery, there were 470 cases (54.5 per cent) who have been improved to such an extent that many have already been discharged as "arrested", many are in good condition and are being prepared for discharge, and the remainder have improved from a poor to a good prognosis. Subsequently, a large number of the 66 cases prepared for surgery but not yet operated on, some of the 28 cases having postoperative complications and a few of the 23 cases who have had retreatment with Streptomycin or Dihydrostreptomycin will probably recover.

Any attempt to determine the net gain of our Streptomycin Program is practically impossible at this time. An approximation of the figures for this type of hospital, however, may be made by comparing the combined percentage of recovery of the Streptomycin treated non-surgical cases and the surgical cases whose surgery was made possible solely by the use of Streptomycin, with the percentage of recovery of all moderate and far-advanced cases in previous years who did not have any form of surgery. It may be stated conservatively that over 50 per cent of properly

TABLE II  
Extra-Pulmonary Tuberculosis Treated With Streptomycin

TYPE OF DISEASE	— R E S U L T S —	
	Favorable	Temporary or No Improvement
I Tuberculosis of the mucous membranes		
(a) Tracheobronchitis	29 (52.7%)	26
(b) Laryngitis	72 (69.2%)	32
(c) Enteritis	13 (54.1%)	11
(d) Rectal	6 (100%)	0
II Tuberculosis of bones and joints	7 (63.6%)	4
III Genito-urinary tuberculosis	9 (90 %)	1
IV Tuberculous Lymphadenitis	4 (44.4%)	5
V Broncho-pleural Fistulae	7 (36.8%)	12
VI Tuberculous Meningitis	1 (14.3%)	6
TOTAL	148 (60.4%)	97
GRAND TOTAL		245

selected cases were improved in a permanent way. Since the total number of treated cases represented about 40 per cent of all admissions (after the full scale program was established) the cases receiving permanent benefit were approximately 20 per cent.

If, as the figures seem to indicate, there is real gain in Streptomycin treatment, that gain must ultimately be reflected in a decreased death rate. At the present time, a more obvious indicator is that the hospital stay of some of the treated cases is reduced to about one-half or one-third of the time required for the same type of case left untreated.

One of the greatest problems confronting us at the beginning of our program was the prolongation of lives of hopeless cases for weeks or months, which created serious shortage of beds needed for the more urgent treatable cases. We finally were forced to refrain from treating unmistakably hopeless cases, except as a palliative measure.

Although an absolute clinical improvement was proved rather early in the Streptomycin Program, the pathological changes resulting from Streptomycin treatment in human tuberculosis had to wait some time for an understanding because the material was rather slow to accumulate. The pathology is of two types, viz. that due to toxicity of the drug and that due to the effect of the drug on the tuberculosis.

The pathology of the labyrinth disease is still obscure. Fowler<sup>38</sup> has felt that it is due to the nerve nucleus damage. The effect of the drug on the lesions is more definite, but many features are not yet classified. The effect on the kidney is even more indefinite.

The effect on the lesions in the brain is apparently not constant. Baggenstoss, Feldman and Hinshaw<sup>39</sup> found that in one case there was an apparent stimulation of tubercle formation resulting in a sort of tuberculous encephalitis. They felt this stimulation was due to the low concentration of Streptomycin since they could recover very little Streptomycin from the brain. Rhymer and Wallace<sup>40</sup> confirm these findings. Baggenstoss, Feldman and Hinshaw<sup>39</sup> showed healing of tubercles similar to those found elsewhere in the body. The most complete work on the pathology of the central nervous system is that of Zollinger<sup>41</sup> who showed that a fibroid condition develops in the patients who survive a long time. The fibrous tissue causes a closure of the subarachnoid spaces, resulting in hydrocephalus. An endophlebitis results in a red encephalomalacia, and an endarteritis, a white encephalomalacia. Practically all workers agree that there is marked effect on recent small tubercles. There is a "withering" effect on the monocytic cells around the periphery, a decrease in caseation and a gradual supplanting of the caseous centre by

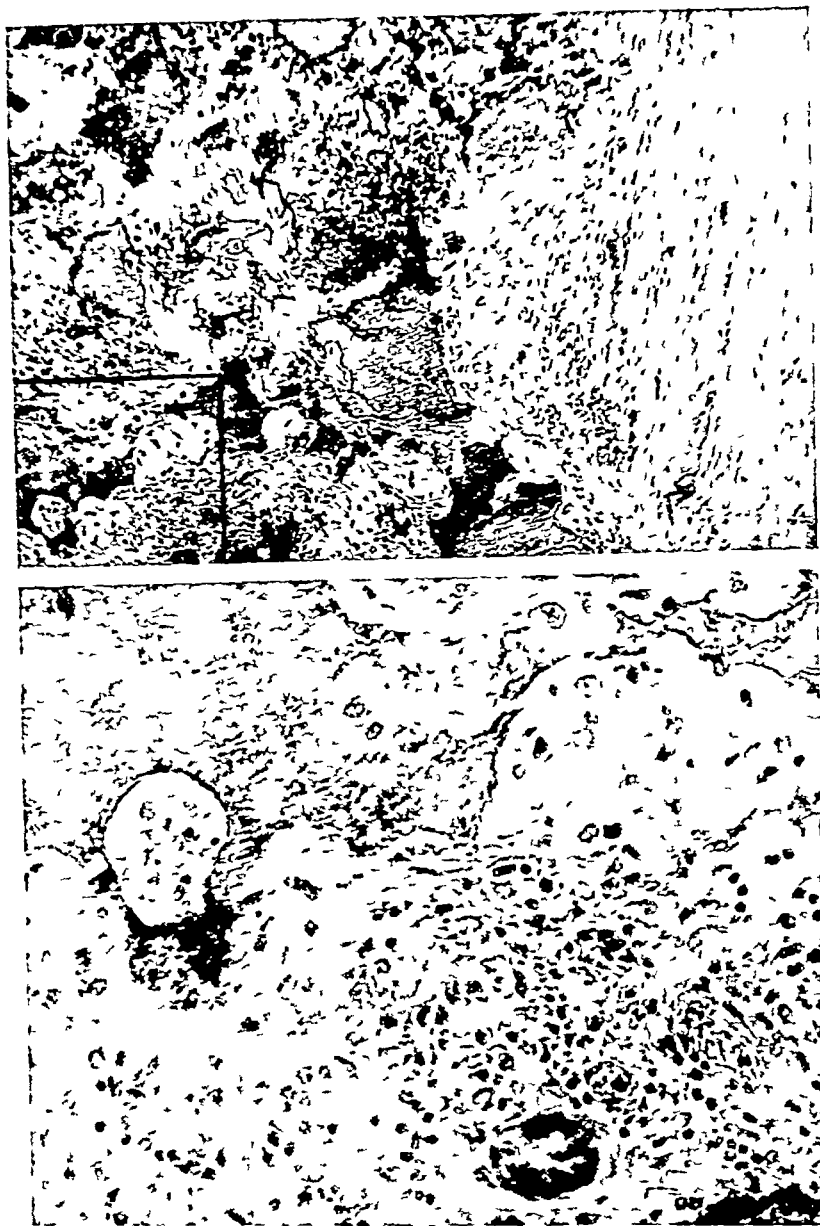


FIGURE 1

*Fig a* A low power view of a calcified hilum lymph node in Case I. Heavy fibrous capsule on the right and broken islands of calcification beneath  $\times 30$  H and E.  
*Fig b* A higher magnification of a portion of *Fig a* outlined in rectangle. Note the invasion of phage cells into the calcified islands, a condition rarely seen before 8-10 years  $\times 200$  H. and E.

fibroblasts and fibrous tissue. Many old tubercles thus healed appear only as scars of fibrous tissue.

The following cases will illustrate several types of change in tubercles from different parts of the body. While the changes in many tubercles are not remarkable, those of primary lesions and those of the liver are rarely seen in ordinary terminal cases.

*Case 1* WB, a three year old white male, was first brought into the Children's Memorial Hospital with what was thought to be a terminal condition, having far-advanced lung disease and draining neck sinuses.

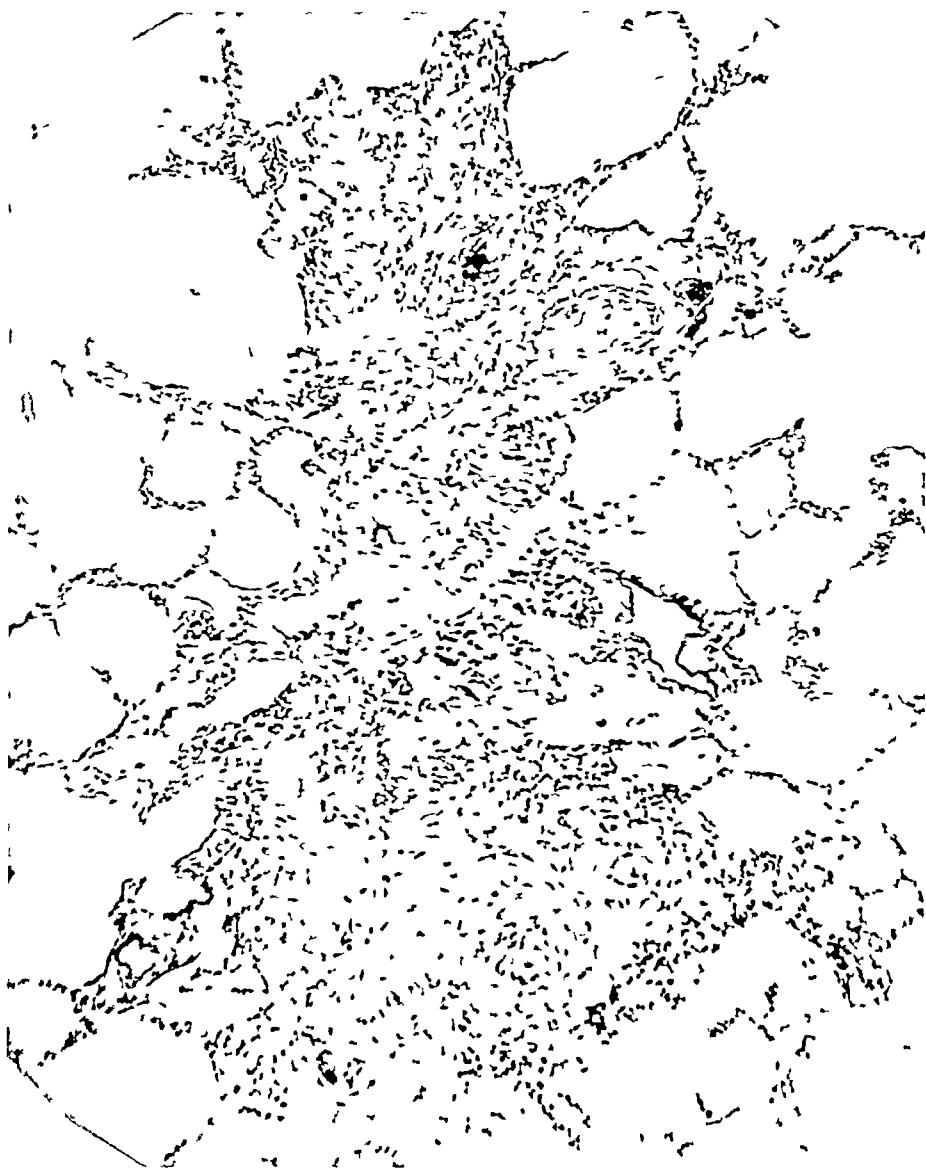


FIGURE 2

A low power view of a miliary tubercle in the lung of the same case. Note the withered epitheloid and giant cells and the replacement of the caseous center with fibroblasts.  $\times 30$  H and E.

He was started on large doses of Streptomycin and almost immediately transferred to our hospital where the treatment was continued but on lower dosage. The almost moribund child gradually improved, became afebrile and alert, gained weight, his sinuses healed and he finally was allowed liberty around the ward. In the meantime, the roentgenograms revealed a considerable clearing in the lungs. Then, suddenly he became nauseated and developed other signs of meningitis, from which he expired within two weeks.

*Necropsy* Death was caused by an ordinary basal meningitis which developed from a Streptomycin resistant strain of tubercle bacilli.

The lungs were remarkable in that they presented marked healing in a far-advanced and ulcerative tuberculosis. There was an excavation of most of the middle lobe with a residue of calcified caseous material around the margins and numerous gravelly concretions in all the interstices of the cavity. The calcified foci appeared to be of greater age than ever seen before in a three year old child. The cavity generally had a smooth wall, some of which was becoming relined with epithelium. Another large and more recent cavity that had contracted to about a third of its former size was present in the right upper lung lobe. There

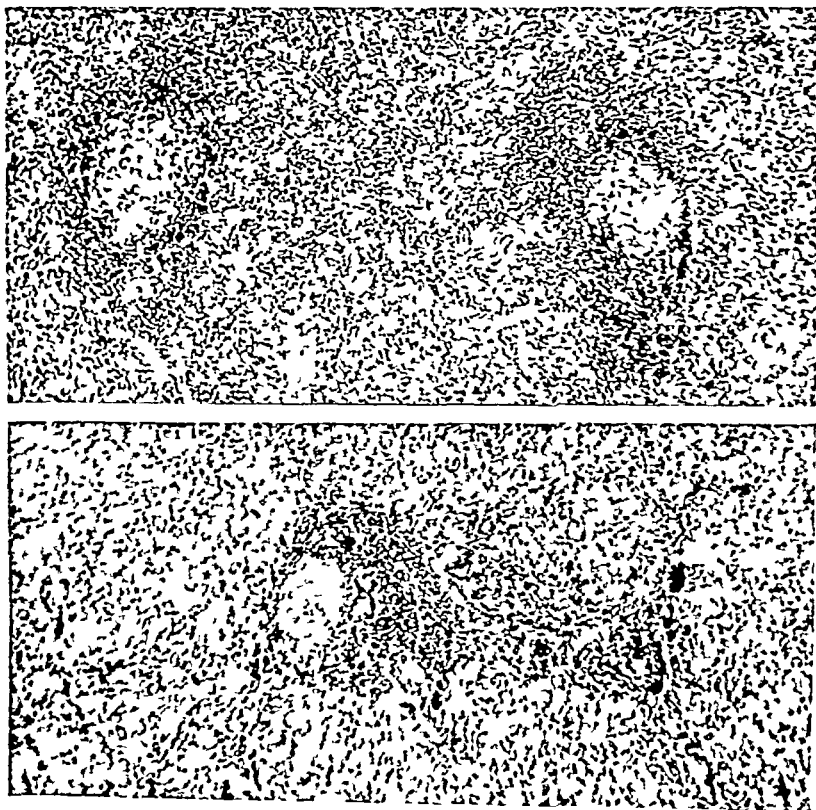


FIGURE 3

*Fig a* A low power view of a section of the spleen of the same case. Note the remnants of miliary tubercles as fibrous tufts in the Malpighian corpuscles.  
*Fig b* Same type of formation in the liver.  $\times 30$  H and E.



was practically no pyogenic layer left, and much fibrosis was present in the walls of the cavity. In the left upper lung lobe there were many tubercles heavily encapsulated and calcified.

*Microscopic Examination* Hilum lymph node tubercle. A decalcified and stained section of a primary hilum lymph node tubercle presented a mass of broken calcified islands with marked resorption, which has been described earlier, and a replacement of the resorbed areas with fibroblasts and capillaries. No bone or fibro-ostoid tissue was present, but the changes were those normally seen only after six to seven years time.



FIGURE 4

A view of the border of an ulcer in the ileum. Note the withered epithelioid cells and giant cells, with lymphocytes beneath the floor of the ulcer.  $\times 50$  H and E.

It was the impression that healing was about twice as rapid as seen in ordinary healing tubercles (Fig 1)

Other changes in the lymph nodes were markedly regressive, with fibrosis and a disappearance of caseation, but were not different from those that have been seen in healing lesions without Streptomycin. The lesions in the lung parenchyma were of two types: the miliary, showing a skeleton tubercle enclosed in the capsule of fibrosis, and almost complete resorption of the caseation. Occasionally there was an obsolete or changed giant cell. The other type, or larger tubercle, seemed to be altered around the periphery, especially if recent, revealing a pyknosis and "withering" of the epithelioid cells but not remarkable in the deeper aspect of the tubercle (Fig 2)

In the spleen were accumulations of lymphocytes with a few interlacing fibroblasts in the malpighian corpuscles which were thought to be healing and healed tubercles. The writer has never before observed as many of these healed lesions in a spleen (Fig 3a)

In the liver there were a few fibroid tufts that presumably were at one time miliary tubercles which had undergone healing similar to the healing described of the lesions in the spleen (Fig 3b)

The gastro-intestinal tract is probably the most interesting, since few reports have been made on healed lesions in these organs. The whole mucosa was a fused mass of stroma, fibroblasts and an occasional "blind" duct with only a few mucosal cells remaining. A small ulcer with overhanging edges had a few old giant cells around the margins but only a slight infiltration of lymphocytes in the base of the ulcer. The whole picture was that of removal of inflammatory elements with little or no replacement of fibrous tissue.

It was the feeling that the healing present had been speeded greatly by the treatment with Streptomycin (Fig 4)

*Case 2* A 55 year old male was ill with tuberculosis since January 1946 and was treated with pneumothorax in 1946 and with thoracoplasty on the right side in 1947. In July 1948 he had a spread to the left lung and in addition he had a tuberculous epididymitis (Streptomycin 0.5 gm daily) was begun on August 24, 1948, and continued until October 26, 1948. There was a considerable improvement but on December 6, 1948, he developed signs of meningitis (rigidity of the neck, positive Kernig, etc.), and on December 8, 1948, treatment with Dihydro-streptomycin was begun, 3 gm daily and 25 micrograms intrathecally three times a week. He expired nine days later.

The essential features were a post-thoracoplasty right lung, with a "healing emphysema" in the left lung. The tubercles were mostly dry, caseous and encapsulated. The epididymis were both filled with caseation and free flowing pus. The vas deferens on each side also contained pus. There were many small nodules in the kidneys. The cerebellum contained several yellow gray areas of several mm in diameter. The largest measured 12 mm in greatest dimensions. The other organs presented nothing remarkable.

The tubercles in the liver especially showed a remarkable degree of fibrosis. A heavy band of collagenous connective tissue was present around a small area of pale caseous material. In fact, some of the tubercles were almost entirely filled with fibrous tissue. The tubercles in the lungs appeared to be undergoing healing but there was nothing that would not be found in any healing tuberculous process.

The cerebellar tubercles were rather unusual in that the periphery of monocytes had a "scorched" or "frost bitten" appearance with some fibroblasts beginning to form around the outer margin. The impression was gained that the effect was recent and perhaps due to the Streptomycin.

### *Discussion*

One of the remarkable features of Streptomycin studies is the rapidity with which the work is progressing. Every week brings out some new and improved aspect of the treatment. Already, Dihydro-streptomycin is being prepared in quantity and has been found to produce little or no ear damage in doses less than 2 grams a day. Dihydro-streptomycin, however, according to work of Feldman and others<sup>42</sup> does not insure protection against resistance to Streptomycin. Other combinations of drugs are being used to supplement Streptomycin when resistance to the drug prevents further curative effect. Sulphones have been used by Debré,<sup>24</sup> Cocchi<sup>23</sup> and others, and promizole has been used in meningitis by Lincoln.<sup>43</sup> Iodides have been used by Woody and Avery<sup>44</sup> in chronic tuberculosis. We have used Paramino-salicylic acid with some success after Streptomycin has failed. Vannesland, Ebert and Block<sup>45</sup> have shown experimentally that the use of P A S with Streptomycin is better than that of either drug alone. It is desirable that an accessory drug be found to take over the action by the time the bacillus has gained resistance to Streptomycin.

Before closing, a few words of caution should be offered. First is a warning against too large a dosage of Streptomycin. The trend from the beginning has been to reduce both dosage and time of treatment. The dosage we use approaches an ideal where the greatest benefit is obtained with the least damage. This work has supported the work of others<sup>24, 20</sup> who have reported that good results can be obtained by 0.5 to 1.0 gram dosage. While those who have had adequate experience with the drug have already learned how to avoid most ear complications, all too many have continued to give as large as two to three grams daily, which is almost certain to leave cripples even if the disease is controlled. Furthermore, it is not yet safe to rely too much on Dihydro-streptomycin because it is not always exempt from danger, especially in dosage over two grams a day.

Much more serious is the problem of germ resistance. We cannot escape the conclusion that after a few years our new infections will be due largely to resistant bacilli for which no remedy is now available. Already some cases are appearing. Therefore, the random use of Streptomycin on minimal lesions or fibro-ulcerative types in which the indications are slight or dubious, as judged by

vast experiments already performed, should be discouraged and where possible forbidden. Exception should be made when such cases are amenable to surgery, for the drug may here be used with advantage, both in preparing the patient and in prevention of post-surgical exacerbation of the tuberculosis.

The final results of Streptomycin treatment are still speculative, but enough has already been accomplished to aid materially in the solution of the tuberculosis problem, and it is not too much to expect a still better method of therapy within five years or less.

No better concluding remarks could be made than to repeat the words of Waksman,<sup>3</sup> namely "A turning point has now been reached in the chemotherapy of tuberculosis. Although Streptomycin may not be the final answer in the treatment of this scourge of mankind—and I hope that it is not—it has opened a new path of antibiotic approach to chemotherapy, an approach sought since the discovery of the bacterial nature of the disease, the control of tuberculosis may finally materialize and thus advance man one step further in his battle against disease and epidemics."

### SUMMARY AND CONCLUSIONS

A brief and incomplete summary of the beginning and development of Streptomycin work over the world, including important features of our own work, has been presented. The essential features may be enumerated as follows:

1) Streptomycin "suppresses" the growth of practically all strains of tubercle bacilli for periods of several weeks to several months.

2) During that period of time there is a large number of cases changed from poor to a good prognosis, this will be reflected ultimately in a lowered death rate and a shortening of the time of individual convalescence.

3) Resistance to Streptomycin develops partially or completely in about 80 per cent of strains of tubercle bacilli on or before 120 days of treatment.

4) Recently formed lesions (probably those retaining blood circulation) respond the most favorably to treatment with Streptomycin, lesions respond less favorably as they become more caseous or more fibroid in character.

5) At the present time, indications are that the optimum dosage of Streptomycin is around one gram a day, although 0.5 of a gram a day has been used with success.

6) In our work we have used a dosage regimen of 0.5 gram a day on adult patients under 150 pounds, and 0.75 gram a day on those over 150 pounds, for 45 to 120 days or up to the time of development of bacillary resistance. In infants and children under

50 pounds 0.1 to 0.3 grams has been found adequate. Only one case of labyrinth disease has developed on this regimen.

7) Of 863 cases in which treatment was completed, using the 0.5 to 0.75 gram dosage, 470 cases (54.5 per cent) were improved in a substantial and more or less permanent way, have gone on to recovery, are progressing towards recovery, or have undergone surgery.

8) There were 670 (77.6 per cent of all cases) non-surgical cases, 425 of which were pulmonary (63.3 per cent of the latter group and 49.3 per cent of all cases). Of these pulmonary cases, 223 (52.5 per cent of the group and 25.9 per cent of all cases) were improved. Of the remainder of the non-surgical cases, 245 (28.3 per cent of all cases) were non-pulmonary, with 148 (60.4 per cent of the latter and 17.2 per cent of all cases) showed improvement.

9) Surgery was recommended in 193 (22.4 per cent of all treated) cases, of which 99 have been operated on successfully and 28 have been operated on but have had postoperative complications, 66 cases have refused surgery or the operation has been delayed for one reason or another.

10) On meningeal, miliary, bone, joint and genito-urinary lesions, 1.0 to 1.5 grams of Streptomycin is still recommended, but Dihydrostreptomycin in doses up to two grams is preferred because of its lower neuro-toxicity.

11) The basic pathologic change in the tubercle is in the reduction of monocytes and epithelioid cells, the decrease and perhaps cessation of caseation with a gradual fibrotic replacement of the central caseation and a thickening of the capsule of the tubercle. In primary calcified tubercles there is a marked acceleration of calcification and resorption of the calcification with replacement by fibroblasts, collagenous tissue and capillaries.

12) In the lesions of the intestinal mucosa where the epithelium is largely destroyed, the first changes observed are the disappearance of acute inflammatory cells and a withering of the epithelioid and giant cells from the floors of the ulcers with only a few lymphocytes remaining. Later changes have not yet been observed, but it is presumed that fibroblasts and fibrocytes appear in order and ultimate re-epithelialization takes place.

13) The types of lesions in the central nervous system are quite varied, depending on many factors such as the type of the disease, duration of the disease before treatment, the development of fibrous tissue, and development of bacillary resistance. In partly healed lesions fibrous tissue may block the subarachnoid spaces, causing hydrocephalus, basilar endarteritis and endophlebitis may lead to white and red encephalomalacia respectively. Small tubercles may heal by fibrosis as do lesions elsewhere in the body or

there may be exacerbations of caseous and fibrocaceous lesions in the meninges, mostly in its basal region

14) There is nothing specific in the pathologic changes caused by Streptomycin

### RESUMEN Y CONCLUSIONES

-Se presenta un breve e incompleto resumen de los comienzos y evolución del trabajo sobre la Estreptomicina en el Mundo, incluyendo los hechos importantes de nuestro trabajo personal

Los puntos esenciales pueden ser enumerados como sigue

1) La Estreptomicina "suprime" el crecimiento de practicamente todas las cepas de bacilos tuberculosos por periodos desde varias semanas hasta varios meses

2) Durante este periodo de tiempo hay un gran numero de casos que cambian de malo a buen pronostico, esto se reflejara a la postre en una mortalidad menor y en acortamiento del tiempo de la convalescencia individual

3) La resistencia a la Estreptomicina se desarrolla parcial o completamente en aproximadamente 80 por ciento de las cepas del bacilo tuberculoso dentro o antes de 120 dias de tratamiento

4) Las lesiones recién formadas (probablemente las que conservan circulacion sanguínea) responden mas favorablemente al tratamiento con Estreptomicina, las lesiones responden menos favorablemente a medida que son mas caseosas o de carácter mas fibroso

5) En el momento actual hay indicaciones de que la dosis optima de Estreptomicina es alrededor de 1 gmo por dia aunque 0.50 por dia se ha usado con exito

6) En nuestro trabajo hemos usado una dosificacion de 0.50 gms por dia en enfermos pesando menos de 150 libras y 0.75 gms por dia en los que sobrepasan 150 libras, por 45 a 120 dias o hasta que se desarrolla la resistencia bacilar En bebes y en niños con menos de 50 libras 0.10 a 0.30 se ha encontrado adecuado Solo se ha encontrado un caso de afección del laberinto con esta dosificacion

7) De 863 casos en los que el tratamiento se ha terminado usando la dosificacion de 0.50 a 0.75 gms, 470 (54.5 por ciento) mejoraron de un modo evidente y de modo mas o menos permanente, han marchado hacia la recuperacion, estan en vias de obtenerla o se han sujetado a la cirugia

8) Hubo 670 (77.6 por ciento) de todos los casos no quirurgicos, de los cuales 425 eran pulmonares (63.3 por ciento del ultimo grupo y 49.3 por ciento de todos los casos) De estos casos pulmonares 223 (52.5 por ciento del grupo y 25.9 por ciento de todos los casos) no eran pulmonares, con 148 (60.4 por ciento de los

ultimos y 17 2 por ciento de todos los casos) que mostraron mejoría

9) Se recomendó la cirugía a 193 (22 4 por ciento de todos los tratados) de los que 99 han sido operados con éxito y 28 han sido operados, pero tuvieron complicaciones postoperatorias, 66 rehusaron las operaciones o la operación ha sido diferida por una u otra causa

10) En la tuberculosis meníngea, miliar, ósea, articular y genito urinaria se recomiendan aun dosis de 1 00 gmo a 1 50, pero la Dihidroestreptomycin en dosis hasta de 2 gmos es preferida por su neurotoxicidad más baja

11) El cambio histológico en el tubérculo básicamente es la reducción de los monocitos y de las células epiteloides, el decrecimiento y quizás la suspensión de la caseificación con una sustitución por fibrosis de la caseificación central y el engrosamiento de la cápsula del tubérculo En los tubérculos primarios hay una marcada aceleración de la calcificación y reabsorción de la calcificación con sustitución por fibroblastos, tejido colágeno y capilares

12) En las lesiones de la mucosa intestinal donde el epitelio es ampliamente destruido, los primeros cambios observados son la desaparición de las células inflamatorias agudas y el decrecimiento de las celdillas epiteloides y gigantes en el fondo de las úlceras, quedando solo algunos linfocitos Cambios ulteriores no se han observado aun pero se supone que aparecen fibroblastos y fibrocitos y que después se realiza una re-epitelización

13) Los tipos de lesiones del sistema nervioso central son muy variados, dependiendo de muchos factores tales como el tipo de la enfermedad, duración de ella antes del tratamiento, el desarrollo de tejido fibroso y el desarrollo de resistencia bacilar En las lesiones parcialmente curadas el tejido fibroso puede bloquear los espacios subaracnoideos, causando hidrocefalia, la endarteritis y la endoflebitis basilar pueden conducir a encefalomalacia blanca o roja respectivamente Los pequeños tubérculos pueden curar por fibrosis como las lesiones en cualquier parte del cuerpo o puede haber exacerbaciones de lesiones caseosas o fibrocaseosas en las meninges, especialmente en su región basal

14) No hay nada específico en los cambios patológicos producidos por la Estreptomycin

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# A Synthesis of the Prevailing Patterns of the Bronchopulmonary Segments in the Light of Their Variations\*

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During the last four years the writer and his associates have been analyzing and mapping the arrangement and distribution of bronchial and vascular trees within the lungs, lobe by lobe. At least fifty specimens of each lobe (and in some cases a hundred or more) have been carefully dissected and sketched. These, in turn, have been supplemented by fresh specimens injected with colored gelatins.

Hitherto, published figures have been faithful replicas of original specimens, but now for purposes of instruction it has seemed desirable to create a hypothetical pair of lungs that would combine the prevailing patterns of all the segments—assembly drawings, as it were, to illustrate not only the arrangement of structures at the hilum, but also the projections onto the surface of the principal bronchi.

Probably such "ideal" specimens are only occasionally encountered, for a variation in even one zone necessarily modifies the development of adjacent segments, and the lungs are the most plastic of all organs. Hence the greater need for an empirically established pattern by which deviations may be judged. Accordingly these plates are presented in the hope that when the simpler plan has been mastered the reader will turn to the studies listed in the bibliography for a more detailed record of the struggle for space that has been waged by the embryonic bronchial buds.

Figure 1 shows an orthodox plan of the bronchial tree with ten major (i.e. segmental) bronchi on the right and nine on the left. The reduction in number of segments in the left lung is due to the union of apical and posterior bronchi ( $B^1$  plus  $^3$ ). As will be pointed out later, this change involves much more than possession of a common stem, namely an "elision" of these bronchi. Many authors also consider that the medial basal and anterior basal bronchi of the left lung ( $B^7$  and  $B^8$ ) aerate a single segment. But in a study of sixty left lower lobes<sup>1</sup> it has been shown that these two bronchi maintain their identity and do not form a composite stem as so often happens in the case of  $B^1$  plus  $^3$ .  $B^7$  has merely

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shifted its position laterally. The fact that it has a common stem with  $B^8$  is no more pertinent than that the middle lobe bronchi ( $B^4$  and  $B^5$ ) have a common stem. In fact there is more reason for considering the middle lobe a single segment.

### *The Right Upper and Middle Lobes*

These two lobes are frequently fused, especially on the mediastinal surface. Together they may be compared to the left upper lobe, each large unit containing five segmental bronchi.

The mode of branching of the *upper lobe bronchus*<sup>7</sup> is prevalently trifurcate (46 per cent of fifty specimens) but the bronchus is subdivided into  $B^1$ ,  $B^2$  and  $B^3$  (figs 2 and 5) in only 38 per cent. The 54 per cent of bifurcate types may be divided into four more or less equal groups—namely three in which  $B^1$  or  $B^2$  or  $B^3$  (or most of each bronchus) forms one of a pair of trunks, and a fourth (the quadrivial type) in which  $B^3$  splits into two components, the  $B^3a$  ramus arising in conjunction with  $B^1$ , and the  $B^3b$  ramus in

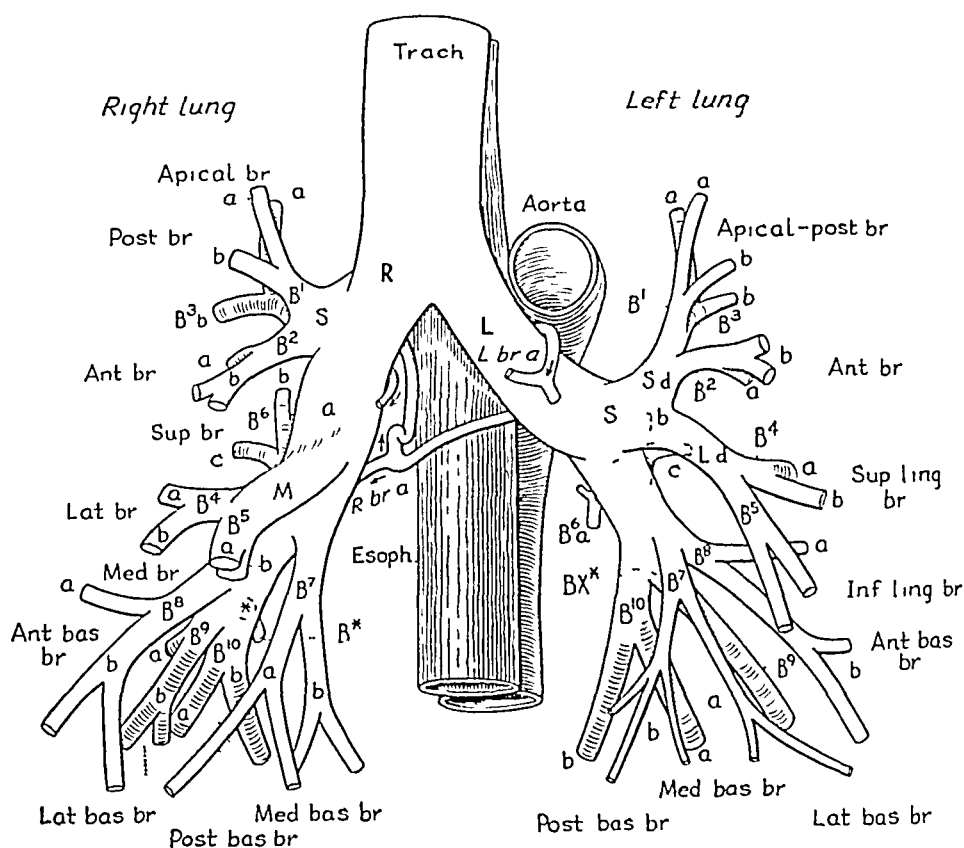


FIGURE 1. Anterior view of bronchial tree, illustrating prevailing mode of branching of segmental bronchi (Modified from Boyden, Surgery, 1945). S, M (of right lung), superior and middle lobe bronchi, Sd, Ld (of left lung), superior and lingular (inferior) divisions of upper lobe bronchus,  $B^*$ ,  $BX^*$ , sub-superior and accessory subsuperior bronchi,  $B^1$ ,  $B^2$ , etc., apical and anterior segmental bronchi, etc., a, b, their principal rami.

conjunction with  $B^2$ . Also, of special interest are the 28 per cent of cases in which  $B^{1b}$  arises as an accessory branch ( $BX^{1b}$ ) of  $B^2$ . In such anomalies, pus from an apical lesion could discharge through the orifice of the anterior segmental bronchus, and, of course, the size of the anterior segment would be greatly increased.<sup>11</sup> For rarer or less striking variations, and for patterns and variation of arteries and veins, the reader is referred to Reference 7.

A preliminary study of the *middle lobe bronchus*, based as yet on only 33 specimens,<sup>5</sup> suggests that the principal bronchial variation centers around the inferior ramus of the medial segmental bronchus—the one which supplies the diaphragmatic surface of the middle lobe ( $B^{5b}$ , figs 2, 5 and 10). It may arise in conjunction with the lateral segmental bronchus ( $B^4$ ), or as an accessory branch of it, or even as one of three bronchi into which the middle lobe stem trifurcates. Incidentally, the plane which separates medial and lateral segments is crossed more frequently by large arteries than in any other pair of adjacent segments (53 per cent of 33 specimens). For arrangement of vessels, see Reference 2.

### *The Left Upper Lobe*

The mode of branching of the left upper lobe bronchus, in contrast to that of the right is prevailingly bifurcate. In 73 per cent of 100 specimens<sup>4</sup> it divides into a superior and an inferior (lingular) division. In the large remainder (27 per cent) it trifurcates into a modified upper division, an anterior bronchus ( $B^2$ ) and a lower (lingular) division.<sup>6</sup> This is due to one of two processes—either to a downward displacement of  $B^2$  or to a splitting of  $B^2$  with downward displacement of its larger inferior component—the upper component remaining as an accessory anterior bronchus ( $BX^2$ ) at the usual site.

This *splitting of the anterior bronchus*—i.e., its embryonic origin from two bronchial buds instead of one—is vital to an understanding of the left upper lobe. The process occurs in 33 per cent of 100 specimens.<sup>4</sup>

Another significant variation, frequently associated with the splitting of the anterior bronchus, is the *downward displacement of the anterior ramus of the apical bronchus* ( $B^{1b}$ ). In 38 per cent of 100 specimens<sup>4</sup> it develops as an accessory ramus ( $BX^{1b}$ ) of  $B^2$  (or of  $BX^2$ ). Such a shifting of  $B^{1b}$  provides a bronchial pathway (on the left side as on the right) by means of which a diseased process in the apex can involve a major portion of the lobe in an appreciable number of lungs. As a result of these two processes, the anterior segment is either greatly enlarged (11 per

cent) or reduced to at least half of its normal size (33 per cent) <sup>10</sup>

A third important variation<sup>6</sup> is the *absence of the posterior ramus of the anterior segment*, B<sup>2</sup>a, (in 35 per cent of 100 specimens<sup>4</sup> and its replacement by BX<sup>2</sup>a, an accessory ramus of the lingular division (12 per cent of specimens) <sup>4 10</sup> This anomalous branch and its artery constitutes an anatomical hazard to lingulectomy <sup>3</sup>

A fourth variation is the deeply *cleft left upper lobe* It has been observed in 8 per cent of 100 specimens <sup>4</sup> The "middle lobes," thus formed have been classified into four types 1) a true middle (or lingular) lobe, 2) a compressed lingular lobe, 3) an expanded lingular lobe, and 4) the ectopic arterial type associated with the occurrence of an ectopic pulmonary artery

#### EXPLANATION OF FIGURES, PLATE I)

(Sketches rendered for publication by Lawrence B Benson)

Prevailing patterns of the bronchopulmonary segments of the right upper and middle lobes, and of the left upper lobe

#### SEGMENTAL BRONCHI

<i>Superior lobe (Right)</i>	<i>Superior division (left superior lobe)</i>
B <sup>1</sup> - <i>Apical bronchus</i>	B <sup>1</sup> plus 3 - <i>Apical-posterior bronchus</i>
B <sup>1</sup> a - apical ramus	B <sup>1</sup> a, B <sup>3</sup> a - apical rami
B <sup>1</sup> b - anterior ramus	B <sup>1</sup> b, B <sup>3</sup> b - anterior and posterior rami
B <sup>2</sup> - <i>Anterior bronchus</i>	B <sup>2</sup> - <i>Anterior bronchus</i>
B <sup>2</sup> a - posterior ramus	B <sup>2</sup> a - posterior ramus
B <sup>2</sup> a 1 - superior subramus	
B <sup>2</sup> a 2 - inferior subramus	
B <sup>2</sup> b - anterior ramus	B <sup>2</sup> b - anterior ramus
B <sup>3</sup> - <i>Posterior bronchus</i>	
B <sup>3</sup> a - apical ramus	
B <sup>3</sup> b - posterior ramus	
<i>Middle lobe (Right)</i>	<i>Inferior (lingular) division (Left)</i>
B <sup>4</sup> - <i>Lateral bronchus</i>	B <sup>4</sup> - <i>Superior lingular bronchus</i>
B <sup>4</sup> a - posterior ramus	B <sup>4</sup> a - posterior ramus
B <sup>4</sup> b - anterior ramus	B <sup>4</sup> b - anterior ramus
B <sup>5</sup> - <i>Medial bronchus</i>	B <sup>5</sup> - <i>Inferior lingular bronchus</i>
B <sup>5</sup> a - superior ramus	B <sup>5</sup> a - superior ramus
B <sup>5</sup> b - inferior ramus	B <sup>5</sup> b - inferior ramus

Note that in the left lung (figs 3 and 4) the anterior segment extends along the anterior margin between the apical-anterior notch and the first notch of the cardiac incisure In the right lung (figs 2 and 5) it begins lower down between the first and second thirds of the anterior margin In the right upper lobe (fig 5) the line between the anterior and posterior segments approximates the junction between the oblique (interlobar) and horizontal (secondary) fissure, but it tends to overlap the latter In the left upper lobe (fig 4) three posterior rami supply the interlobar surfaces, B<sup>3</sup>b, B<sup>2</sup>a and B<sup>4</sup>a In the left apical region B<sup>1</sup> plus 3 forms a single segment (fig 3) Usually it divides into B<sup>1</sup> and B<sup>3</sup> to aerate separate subsegments, but frequently B<sup>1</sup>b arises from B<sup>2</sup> and B<sup>3</sup>b slides down the stem of B<sup>1</sup> plus 3 to arise near its base B<sup>1</sup>a usually heads for the subclavian crest B<sup>1</sup>b for the apical-anterior notch (fig 3) In the middle lobe B<sup>5</sup>a may be found by locating the artery (A<sup>5</sup>a) which underlies the medial side of the anterior crest (fig 2), B<sup>5</sup>b runs on the inferior side of the lobe, just lateral to the frenum Final naming of the B<sup>4</sup> awaits study of a larger number of specimens At times the two rami have a superior-inferior relationship





In closing this résumé of the left upper lobe, the *variability of the apical-anterior segment* should be emphasized. Mention has already been made of the displaced B<sup>1b</sup>. Similarly, B<sup>3b</sup> tends to slide down the stem of B<sup>3</sup>, so that in 36 per cent of specimens,<sup>6</sup> the apical-anterior bronchus divides into B<sup>3b</sup> and B<sup>1</sup> plus<sup>3a</sup>. For variations of arteries and veins the reader is referred to Reference 6.

### *The Right Lower Lobe*

Posteriorly, the lower lobes may be divided into three transverse zones (figs 8 and 9), namely a superior segment (B<sup>6</sup>), a layer of basal segments (B<sup>7-10</sup>) and an interpolated subsuperior zone which, because of the variability of its bronchial components, has been given the designation B\* (and/or BX\*)<sup>2</sup>

On the right side (fig 6) the *superior segmental bronchus* bifurcates, (86 per cent of 50 specimens) into a lateral (B<sup>6c</sup>) and superior and medial (B<sup>6b</sup>+a) ram<sup>12</sup>. Because B<sup>6a</sup> is usually a small ramus the superior segment usually caps the basal segments horizontally (62 per cent of specimens). In most of the remainder, B<sup>6a</sup> invades the lower paravertebral surface, giving rise to an oblique capping. In such specimens it would be more difficult to resect the superior segment. Incidentally, the line between B<sup>6c</sup> and B<sup>6a</sup> on the anterior surface (fig 6) usually coincides with the interfissural crest—a low ridge that separates the impressions made by upper and middle lobes. Other details of the ram<sup>1</sup> of B<sup>6</sup> may be found in Reference 12.

The *subssuperior bronchus* (B\*) is a dorsal ramus which grows out of the stem bronchus a varying number of centimeters beneath the superior bronchus (figs 1 and 6). Next to B<sup>6</sup> it is said to be most vulnerable to aspirated material. It has been found in 62 per cent of 50 specimens. Almost always it aerates the posterior sector of the costal surface above B<sup>10</sup> (fig 9), but frequently it spreads medially or laterally. When absent, as such (38 per cent), its place is taken by the accessory subsuperior (BX\*)—a high dorsal branch of B<sup>10</sup>. In 48 per cent, both the subsuperior proper (B\*) and the accessory ramus BX\*(10) are present in the same specimen (fig 9). Since one or both of these occur in every specimen, the interpolated subsuperior zone is a characteristic feature of the right lower lobe.

The *basal segmental bronchi* are four in number. The medial basal (B<sup>7</sup>) is the highest branch (fig 1), the lateral basal (B<sup>8</sup>) is next and then the common stem of the lateral basal and the posterior basal (B<sup>9</sup> and B<sup>10</sup>). All of these reach the diaphragm (fig 10).

The *medial basal segmental bronchus* (B<sup>7</sup>) is of special interest as representing the infracardiac bronchus of mammalian quad-



rupeds, in which animals it forms a separate lobe occupying the space between the heart and diaphragm. In man, the corresponding segment is often separated from the anterior basal (36 per cent) by a supernumerary fissure of varying depth (fig 6). The segment usually occupies the antero-medial portion of the lobe (78 per cent) being represented on both anterior and paravertebral surfaces (figs 6 and 9). It is thus placed athwart the other basal segments (fig 10). These segments, in turn, obliquely overlap each other. Anteriorly, the segment is grooved by the inferior vena cava. In 14 per cent of specimens the segmental bronchus ( $B^7$ ) is absent as such, being represented by accessory ramus of adjacent segments ( $B^8$  or  $B^+$ ). In another 8 per cent it is wholly anterior in its distribution.<sup>12</sup>

The *anterior basal segmental bronchus* ( $B^8$ ) is remarkably con-

# EXPLANATION OF FIGURES, PLATE 2

(Sketches rendered for publication by Lawrence B. Benson)

Prevailing patterns of bronchopulmonary segments of the lower lobes

## SEGMENTAL BRONCHI

### *Right inferior lobe*

$B^6$  - Superior bronchus

$B^{6a}$  - medial ramus

$B^{6b}$  - superior ramus

$B^{6c}$  - lateral ramus

$B^*$  - Subsuperior bronchus

$BX^*$  (10) - accessory  
subsuperior bronchus

$B^7$  - Medial basal bronchus

$B^{7a}$  - anterior ramus

$B^{7b}$  - medial ramus

$B^8$  - Anterior basal bronchus

$B^{8a}$  - lateral ramus

$B^{8b}$  - basal ramus

$B^9$  - Lateral basal bronchus

$B^{9a}$  - lateral ramus

$B^{9b}$  - basal ramus

$B^{10}$  - Posterior basal bronchus

$BX^*$  (10) - accessory  
subsuperior ramus

$B^{10a}$  - laterobasal ramus

$B^{10b}$  - mediobasal ramus

### *Left inferior lobe*

$B^6$  - Superior bronchus

$B^{6a}$  - medial ramus

$B^{6a} 1$  - paravertebral branch

$B^{6a} 2$  - posterior branch

$B^{6b}$  - superior ramus

$B^{6c}$  - lateral ramus

$B^*$  - Subsuperior bronchus

$BX^*$  (9),  $BX^*$  (10) - accessory  
subsuperior bronchus

$B^7$  - Medial basal bronchus

$B^{7a}$  - lateroanterior ramus

$B^{7b}$  - medioanterior ramus

$B^8$  - Anterior basal bronchus

$B^{8a}$  - lateral ramus

$B^{8b}$  - basal ramus

$B^9$  - Lateral basal bronchus

$BX^*$  (9) - accessory  
subsuperior ramus

$B^{9b}$  - basal ramus =  $B^9$

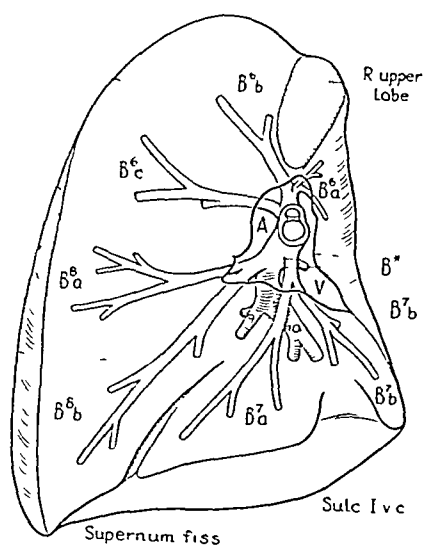
$B^{10}$  - Posterior basal bronchus

$BX^*$  (10) - accessory  
subsuperior ramus

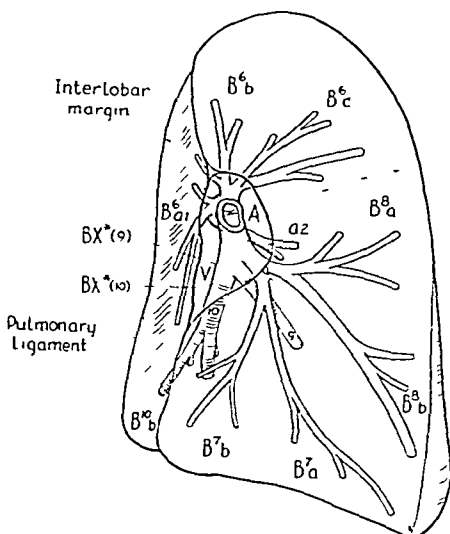
$B^{10a}$  - laterobasal ramus

$B^{10b}$  - mediobasal ramus

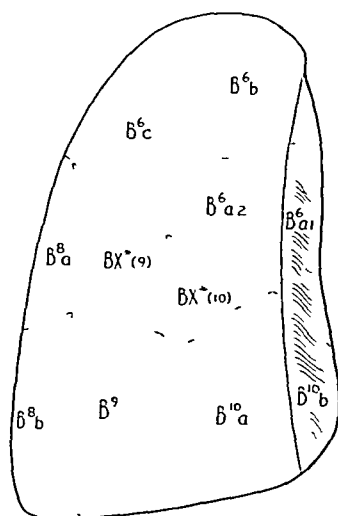
Note that on the right side (figs 6 and 9) the superior segment caps the basal segment horizontally, on the left side (figs 7 and 8), obliquely. Also note that  $B^{6a}$  on the left has a posterior branch ( $B^{6a} 2$ , fig 7). On the right the sub-superior zone is prevailing in the posterior sector of the costal surface (fig 9) and is formed by both the subsuperior proper ( $B^*$ ) and an accessory subsuperior ( $BX^*$ ) from the top of  $B^{10}$ , on the left side (fig 8) the zone lies primarily in the posterolateral sector and is usually formed by accessory subsuperiors ( $BX^*$ ) from the top of  $B^9$  and  $B^{10}$ . In only 29 per cent is there a subsuperior proper ( $B^*$ ) on the left side. Finally on the right (fig 9)  $B^{7b}$  extends onto the paravertebral surface A, V, position of interlobar portion of pulmonary artery and of inferior pulmonary vein.



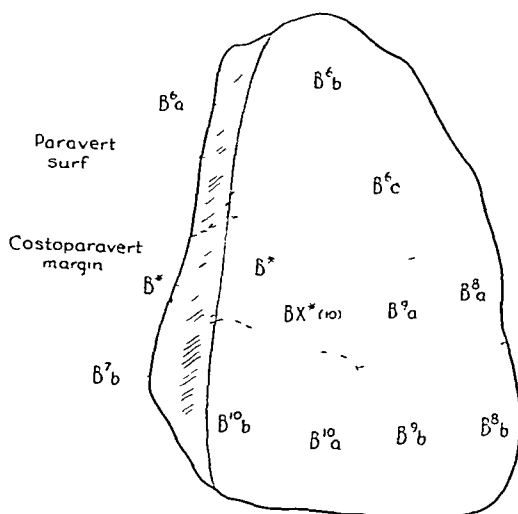
6 RIGHT LOWER LOBE  
(Ant surface)



7 LEFT LOWER LOBE  
(Ant surface)



8 LEFT LOWER LOBE  
(Post view)



9 RIGHT LOWER LOBE  
(Post view)



stant in its division into lateral and basal rami and in the distribution of its lateral ramus ( $B^s a$ , figs 6 and 9) Its basal ramus ( $B^s b$ ) is more variable in distribution since it tends to invade the basal portions of adjacent segments Anteriorly, it occupies the lateral third of the anterior surface, as measured along the inferior margin (50 per cent of specimens, fig 6), but when  $B^r$  is defective it may extend to the sulcus of the inferior vena cava In such specimens (16 per cent),  $B^r a$  develops as an accessory ramus of  $B^s b$  Similarly, when  $B^o$  is absent (8 per cent),  $B^s$  takes over the diaphragmatic portion of that segment ( $B^o b$ , fig 10)  $B^s$ , therefore is one of the dominant segmental bronchi

By contrast, the *lateral basal segmental bronchus* ( $B^o$ ) is less constant It is smaller than the anterior basal and appears to be more like a secondary branch of the posterior basal ( $B^{1o}$ , fig 6) As noted above, it has been found absent, as such, in 8 per cent of specimens Its lateral branch ( $B^o a$ , fig 1) is absent in 14 per cent Its territory is then taken over by the subsuperior ( $B^*$ ) or, less commonly, by  $B^s a$

The *posterior basal segmental bronchus* ( $B^{1o}$ ) is invariably present Its highest dorsal branch, occurring in 86 per cent of specimens, has already been demonstrated to be an accessory subsuperior and redesignated as  $BX^*(10)$  The main bronchus divides into a laterobasal ( $B^{1o} a$ ) and a mediobasal ramus ( $B^{1o} b$ ) The latter is thought by some to represent the termination of the stem bronchus It invariably heads for the inferior medial corner of the lobe (fig 10) For arrangement of vessels, see Reference 2

### *The Left Lower Lobe*

Although possessing units that are comparable to those of the right side, the left lower lobe bronchus (fig 1) presents characteristic differences in mode of branching and in the distribution of its bronchi<sup>1</sup>

The prevailing pattern of the *superior segmental bronchus* (fig 7), although bifurcate (85 per cent of 60 specimens), has the formula  $B^s a$  and  $B^s b+c$  in 43 per cent of specimens This accentuation of its medial ramus ( $B^s a$ ) has two consequences First, because of the downward paravertebral extension of  $B^s a$  (two-thirds or more of the distance to the diaphragm in 57 per cent of specimens) the superior segment usually caps the basal segments obliquely (fig 8) In the right lobe, it is prevaillingly horizontal (62 per cent) Second, the development of a large dorsal branch in 45 per cent of specimens ( $B^s a 2$ , fig 7) displaces the subsuperior zone to a primarily posterolateral sector on the costal surface (fig 8)

The *subsuperior proper* ( $B^*$ ) is present in only 29 per cent (of 60 specimens) as contrasted with the 62 per cent of the right side. It always supplies the posterolateral sector, and may spread to the posterior or lateral sectors, but has never been found paravertebrally as on the right side. It arises a varying number of centimeters below the superior bronchus ( $B^6$ ). Since it determines the characteristic location of the subsuperior zone, any other rami which supply this zone in its absence (or coordinately with it) are designated *accessory subsuperior bronchi* ( $BX^*$ ). These arise as high branches of the lateral basal and posterior basal bronchi—figs 7 and 8,  $BX^*(9)$  and  $BX^*(10)$ . The former occurs in 67 per cent, the latter in 84 per cent of 60 specimens. Since these are more numerous than the subsuperior proper ( $B^*$ ) the prevailing pattern of the subsuperior zone is shown in fig 8 as being made up of the two accessory subsuperiors (43 per cent). Whatever its composition, however—whether consisting of one (22 per cent), two (61 per cent) or three components (17 per cent)—the zone is always present as a potential recipient of aspirated material, next in importance to the superior segment.

The *basal segmental bronchi* ( $B^{7-10}$ ) differ from those of the right lung both in origin and in other substantial respects. The prevailing pattern of the basal trunk (omitting the subsuperiors)

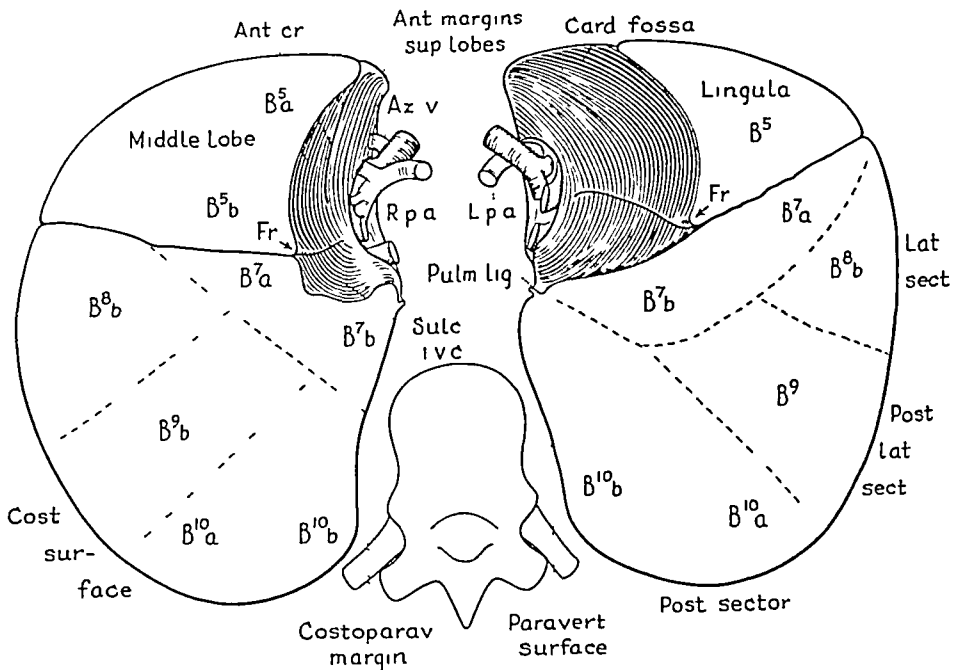


FIGURE 10 Diaphragmatic view of lungs showing distribution of segmental bronchi (Modified, from Berg, Boyden and Smith J Thor Surg, 1949) *Ant cr*, anterior crest of middle lobe rising up to anterior margin, *Az v*, azygos vein, *Fr*, frenum of middle lobe or of left upper lobe, *R p a*, *L p a*, pulmonary arteries, *Sulc i v c*, groove in the anterior surface of the right lower lobe made by the inferior vena cava

is a bifurcation (87 per cent) Most commonly (67 per cent) the trunk divides into  $B^7$  plus  $8$  and  $B^9$  plus  $10$  (fig 7)

The *medial basal segmental bronchus* ( $B^7$ ) has shifted laterally, so that in 87 per cent it arises in common with  $B^8$  or one of its rami (In 10 per cent it arises independently, as on the right side, and in 3 per cent it is absent, as such) Correspondingly the segment which it aerates has shifted laterally, so that prevalingly (55 per cent) it occupies the whole of the inferior anterior surface of the lobe (fig 7)  $B^{10}$  takes over the paravertebral territory vacated by this shift (fig 10) In 20 per cent,  $B^7$  may supply only the medial half to two-thirds of the lower anterior surface and in 22 per cent it may invade the anterior costal territory of  $B^8$

The *anterior basal segmental bronchus* ( $B^8$ ) is far from being the dominant segment that it is on the right side In 70 per cent, it arises in common with  $B^7$ , and in 13 per cent it arises independently In the remaining 17 per cent, either its basal or lateral ramus is absent, as such, in these instances  $B^{8a}$  is taken over by an accessory branch of the subsuperiors, and  $B^{8b}$  by an accessory ramus of  $8^7$  or  $B^9$  In a different 17 per cent the basal ramus fails to reach the diaphragm Prevalingly, the distribution is that shown in fig 7, but in 27 per cent it encroaches upon  $B^7a$  and in 17 per cent it is crowded out of the diaphragmatic and lateral costal area

The *lateral basal segmental bronchus* ( $B^9$ ) occupies the posterior lateral sector of the lobe as on the right side (fig 10), with the exception that its high lateral branch (present in 67 per cent of specimens) supplies the subsuperior zone and hence has been designated  $BX^*(9)$   $B^9$  is absent, as such, in 10 per cent of specimens, its territory being taken over usually by an accessory branch of  $B^7$

The *posterior basal segmental bronchus* ( $B^{10}$ ) is much like that of the right lung except that it takes over the paravertebral zone of  $B^7b$  (figs 8 and 10), and in 30 per cent of specimens a high paravertebral branch is given off before  $B^{10}$  divides into its latero-basal and mediobasal rami For arrangement of vessels, see Reference 2

## DISCUSSION

In concluding this brief resumé of the bronchopulmonary segments, the writer feels that it would be useful to discuss the way in which the above observations differ from those of Brock (1942-44) and of Jackson and Huber (1943)—the two systems which deservedly have obtained greatest recognition in the British Empire and in this country

Aside from the fact that our articles have included a descrip-

tion of segmental arteries, veins and of subsegments, the three series of publications seem to be in general agreement. It is obvious that all three are dealing with the same major branches of the bronchial tree—a statement which does not always apply to older or more recent continental studies.

Jackson and Huber, without publishing the data on which their observations rest, have presented what might be termed the "normal arrangement" of the bronchopulmonary segments, using a terminology of directional terms which is consistent with the Basel Anatomical Nomenclature. While accepting the terms, we would suggest the following minor changes in the disposition of segments. Prevailing, on the right, the medial basal segment ( $B^7$ ) lies on both sides of the pulmonary ligament. On the left, the anterior segment ( $B^2$ ) borders on the interlobar fissure. In the left lower lobe, the anterior-medial basal segment should be separated into its two components,  $B^7$  and  $B^8$ , making a total of nine segments in the left lung. Finally, we feel that it is desirable to recognize a more or less constant subsuperior zone in each lower lobe, even though it cannot be considered to be a segment because of its variable composition.

To Brock we are indebted for an extraordinarily clear, comprehensive and significant account of the anatomy of the bronchial tree. He has related the segments to the thoracic wall, and casts of the tree to bronchographic appearances; he has stressed the importance of "axillary" ramus (first noted by Lucien and Weber) and recorded numerous variations in the extent of the segments. We feel that our work began where Brock left off. By going one step further, i.e. by identifying both the segmental and subsegmental bronchi on the basis of their prevailing distribution and not merely by their origin on the tree, we have obtained an additional tool for interpreting variations. For example, in specimens in which the upper division of the left upper lobe bronchus has only two branches—the lower of which supplies the upper anterior zone (Brock's fig. 50), and the upper of which supplies the apex and the posterior zone—Brock is obliged to call the lower one "apical" and the upper one "subapical." By analyzing the subsegments we can more accurately describe the lower branch as an "accessory anterior" and the upper branch as the apical-posterior bronchus ( $B^1$  plus 3).

In other words, we have applied to the human lung Huntington's concept that the lungs of higher vertebrates are plastic organs and that the primary cause of variations is the opportunistic tendency of bronchial buds to grow into a given zone from more than one point on the embryonic tree. The key to such variations is thus the displacement of ramus.

## DISCUSION

Como conclusión de este breve resumen de los segmentos broncopulmonares, el autor cree que seria util discutir la forma en que las observaciones que anteceden difieren de las de Brock (1942-44) y de Jackson y Huber (1943), los dos sistemas que merecidamente han obtenido mayor aceptacion en el Imperio Britanico y en este País

Fuera del hecho de que nuestros articulos han incluido una descripción de las arterias y venas segmentarias, las tres series de publicaciones parecen en general estar de acuerdo. Es evidente que las tres se refieren a las mismas ramas mayores del arbol bronquial, afirmacion que no siempre puede aplicarse a estudios mas antiguos o mas recientes en Europa

Jackson y Huber, sin publicar los datos en que se basan sus observaciones, han presentado lo que podria llamarse la "forma normal" de los segmentos broncopulmonares usando una terminologia direccional de acuerdo con la Nomenclatura Anatómica de Basilea. Aunque aceptamos los terminos sugeriríamos los siguientes cambios menores en la disposición de los segmentos. Predominantemente, en el lado derecho, el segmento medio basal ( $B^7$ ) se encuentra a ambos lados del ligamento pulmonar. A la izquierda, el segmento anterior ( $B^2$ ) limita con la fisura interlobar.

En el lóbulo inferior izquierdo el segmento basal antero-medio debe ser disgregado en dos componentes  $B^7$  y  $B^8$ , lo que hace un total de nueve segmentos en el pulmón izquierdo. Por ultimo creemos que es deseable que se reconozca una zona subsuperior mas o menos constante, aunque no pueda considerarse como un segmento a causa de su composición variable.

Debemos a Brock una descripción extraordinariamente clara y comprensiva de la anatomía del arbol bronquial. Ha relacionado los segmentos a la pared toracica y las proyecciones del arbol a los aspectos broncograficos, ha insistido sobre la importancia de las ramas "axilares" (primero señaladas por Lucien y Weber) y ha referido numerosas variantes en la extension de los segmentos. Creemos que nuestro trabajo empezo donde Brock lo dejó yendo mas adelante, o sea identificando tanto los bronquios segmentarios como los subsegmentarios basandonos en su predominante distribución y no solamente en su origen troncal, hemos obtenido un recurso adicional para interpretar las variaciones. Por ejemplo en los especimenes en los que la division superior del bronquio del lóbulo superior izquierdo tiene solo dos ramas—la inferior de las cuales corresponde a la zona superior anterior (Brock, Fig. 50) y la superior de la cual corresponde al vertice y



la zona posterior—Brock se ve obligado a llamar la más baja “apical” y la superior “subapical”

Analizando los subsegmentos podemos con más exactitud describir la rama inferior como una “accesoria anterior” y la superior como el bronquio apical anterior ( $B^1$  plus  $3$ )

En otras palabras, hemos aplicado al pulmón humano el concepto de Huntington de que los pulmones de los vertebrados superiores son órganos plásticos y que la causa primaria de las variaciones es la tendencia oportunista de las yemas bronquiales a crecer dentro de una zona determinada desde más de un punto de origen en el árbol embrionario. La clave de tales variaciones es así la presencia de bronquios accesorios o desplazados

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\*Articles marked with an asterisk are based in part upon injection of fresh specimens

# Surgical Treatment of Emphysematous Blebs and Bullae\*

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The first report in medical literature dealing with the subject of cystic disease of the lung is probably that of Thomas Bartholinus<sup>1</sup> found in the Leyden edition of Malpighius in 1687 By 1925 Koontz<sup>2</sup> was able to collect 108 cases in the literature, reported, for the most part, in German medical journals With the development of thoracic surgery and the widespread use of roentgenologic examination of the thorax, interest in this condition has grown steadily By 1936 Schenck<sup>3</sup> was able to report a series of 381 cases collected from the literature and during the last ten years many additional cases have been reported, particularly in American and British journals It has become apparent that cystic disease of the lung is not a rare disease All physicians and surgeons interested in thoracic disease have become familiar with this condition

There is still considerable difference of opinion regarding the proper classification of the various lesions included in cystic disease of the lung, the genesis of these lesions, whether congenital or acquired, and the terms that should be used to describe these lesions It is generally agreed, however, that cystic lesions of the lung can be divided into two chief types those that originate from the bronchial tree and those that are alveolar in origin

Bronchiogenic cysts are characterized by the fact that they possess an epithelial lining of cuboidal or columnar cells which may be smooth and regular, or roughened and trabeculated Bronchiogenic cysts may contain fluid, pus, blood or air alone or in combination Most of the literature on cystic disease of the lung has been concerned with these cysts of bronchial origin Their clinical and roentgenologic manifestations are well known It is universally agreed that they can be treated best by surgical excision

Very little consideration has been given in medical literature to the cystic lesions of the lung of alveolar origin, which include pulmonary blebs, bullae and pneumatoceles Apparently these lesions are not as well understood as the more common cysts of

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bronchial origin and the possibility of benefiting patients with these lesions by surgical means is not appreciated generally. The remainder of this discussion will be devoted to these cysts and their surgical management.

A pulmonary bleb is a localized air pocket situated immediately beneath the parietal pleura. According to Miller,<sup>4</sup> a bleb results from rupture of the subserous layer of connective tissue of the pleura by air from ruptured alveoli separating the pleura proper from the underlying pulmonary tissue. The air extends along tissue planes much as a dissecting aneurysm extends along the wall of an artery.

Bullae and pneumatoceles are located primarily deeper in the lung than are blebs. Maier<sup>5</sup> has defined a pneumatocele as a hyperinflated intrapulmonary cavity produced by the marked distention of a defect in the pulmonary parenchyma. Bullae are believed to result from rupture of dilated alveoli into one another and their coalescence to form intrapulmonary air pockets. I doubt if there is much if any difference between bullae and pneumatoceles. Certainly they cannot be differentiated clinically or roentgenologically, and in the remainder of this discussion I shall use only the terms "blebs" and "bullae." Pulmonary blebs and bullae may be single or multiple. They may involve a single lobe or any combination of lobes. They may occur as a part of a generalized pulmonary emphysema or may occur in any part of a lung in the absence of any detectable evidence of emphysema. They can occur at any age.

The genesis of isolated blebs or bullae in the absence of generalized emphysema is not completely clear. Naclerio and Langer<sup>6</sup> have expressed the belief that they are usually of congenital origin. Undoubtedly in some cases they do originate in this way. However, it is my opinion that localized inflammatory processes involving small bronchi and bronchioles may result in scarring and constriction of these air ducts in such a way that egress of air from the portion of the lung distal to such constriction is interfered with more than the intake of air through the constriction. This process leads to overinflation of the segment of lung involved, rupture of alveolar walls and the development of an air-containing cavity. In other words, localized inflammatory changes may produce changes in the tiny air duct which result in a valvular mechanism in the bronchi. Hayashi<sup>7</sup> has reported finding such valve-like structures on microscopic examination of bronchi leading into pulmonary blebs and bullae, and Allison<sup>8</sup> has recently reported a case in which he was able to demonstrate clearly a valvular action in the bronchus leading to a large air cyst. Allison has also pointed out that bullous cysts may arise

from some overexertion, such as coughing or straining, in the presence of an inflamed or ulcerated bronchus so that rupture of the bronchus occurs at some weak point with escape of air into the interstitial tissues of the lung. For this reason he pointed out that it is not surprising to find bullous cysts in association with bronchiectasis. Freedman<sup>9</sup> has expressed the belief that obstructive processes of the trachea or bronchus, whether due to intrinsic or to extrinsic lesions, may lead to the development of blebs and bullae even in the absence of generalized emphysema. He has also pointed out that air vesicles can result from the presence of foreign bodies and mucinous or pseudomucinous plugs of exudate in the bronchi as well as scarred, constricting lesions of the bronchus.

The chief symptom caused by pulmonary blebs and bullae is dyspnea. They may also produce pain, usually pleuritic in character, and they may become infected, with the development of the usual picture of an infected pulmonary cyst. Cough is not a prominent symptom. The dyspnea in most cases which occurs in patients with blebs and bullae may be of gradual onset and progression as the cysts enlarge, destroying the adjacent pulmonary parenchyma and compressing the remainder of the lung. If the process is extensive enough a patient may even die of asphyxia because of insufficient functioning pulmonary tissue to maintain the respiratory requirements.

Perhaps the commonest manifestation of pulmonary blebs and bullae is the sudden development of dyspnea due to spontaneous pneumothorax. As these blebs and bullae gradually increase in size they reach a point at which their thin walls can no longer withstand the pressure and they rupture into the pleural space, resulting in a completely collapsed lung. Fortunately, high pressure tension pneumothorax with marked shift of the mediastinum does not develop in most cases and if it does occur it comes on gradually over a period of several days. Failure of tension pneumothorax to develop or its slow development can be accounted for by the fact that the bronchial leak is very small in these cases and tension develops slowly or the leak may be closed off when the lung collapses. In the great majority of cases of spontaneous pneumothorax the leak will seal over and the lung will re-expand gradually without any treatment. Roentgenograms of the re-expanded lung often do not show any detectable abnormality of the lung to account for the pneumothorax.

Perhaps a word should be inserted here regarding the etiology of spontaneous pneumothorax. It was once believed that this condition almost invariably resulted from pulmonary tuberculosis. It is now clearly recognized that this is not true and it seems

likely that most instances of spontaneous pneumothorax are due to rupture of pulmonary blebs and bullae Leach<sup>10</sup> has reported a series of 126 cases of spontaneous pneumothorax in air force personnel All of the patients had had negative thoracic roentgenograms previous to the development of the pneumothorax On follow-up in none of the cases could the pneumothorax be proved to be due to tuberculosis Kjaergaard<sup>11</sup> followed 51 patients who had spontaneous pneumothorax and found that in only 1 did evidence of pulmonary tuberculosis develop subsequently There can be little question that tuberculosis is only rarely an etiologic factor in cases of spontaneous pneumothorax In most the lesion is undoubtedly due to rupture of pulmonary blebs and bullae

The treatment of pulmonary blebs and bullae depends necessarily on many factors If the air-containing cavities are multiple and involve both lungs or are a part of a generalized pulmonary emphysema, little can be done for the relief of the patient Small cysts not causing symptoms do not necessarily require any treatment However, the patient should be warned of the potential dangers of such lesions and should be checked frequently by means of thoracic roentgenograms Progressive increase in size warrants consideration of surgical excision if the cyst is solitary or if multiple cysts involve a single lobe or lung Obviously, development of infection in such cysts demands surgical treatment Fortunately, infection does not occur commonly in these lesions Severe dyspnea due to the size of the cyst or due to the development of pneumothorax most frequently demands corrective surgical treatment Needle aspiration of blebs and bullae is definitely contraindicated because it can result only in rupture of the cavity and the production of pneumothorax However, in very large cystic lesions it may be impossible by roentgenologic study to ascertain without question whether the patient has a pneumothorax or a cyst so large that the collapsed lung cannot be identified In instances of severe dyspnea due to a large cystic lesion or a tension pneumothorax it may be necessary as a life-saving measure to insert a needle to aspirate air from the involved pleural space

In instances of spontaneous pneumothorax which from the history appear to be of recent origin, it is the practice of my colleagues and me to observe these patients for several days provided they are not acutely dyspneic in order that the leak in the lung may have an opportunity during the collapsed phase to seal over The lung may gradually expand without intervention If the lung does not begin to re-expand we insert a blunt needle into the pleural space, leave it in place and maintain constant

controlled gentle negative pressure to encourage re-expansion. The needle may be left in place for twenty-four to forty-eight hours, depending on the re-expansion of the lung. If the lung re-expands completely the needle is removed and the condition of the lung is followed by means of daily roentgenograms to be sure that the lung remains expanded and to see if any lesion can be demonstrated that could account for the development of the pneumothorax. If the lung does not re-expand or if after re-expansion it collapses again after removal of the needle, it is assumed that the leak will not close with conservative measures and exploratory thoracotomy is recommended, provided the patient's general condition and particularly the condition of the other lung will permit such an operation. The extent of the surgical procedure that may be necessary varies considerably. Simple repair of a small surface defect has sufficed in some instances, in others lobectomy or segmental resection of a portion of a lobe has been necessary. Rarely, pneumonectomy has been required.

Allison has suggested phrenic nerve interruption as a means of relieving the dyspnea found in some instances of bullous cysts. I have not had occasion to use this procedure as yet but it may have considerable merit. The rationale of this procedure is based on the Hering-Breuer<sup>12</sup> theory of the nervous control of respiration. According to this theory the limits of inspiration and expiration are regulated by the tension within the lung structure and proprioceptive impulses from the lungs, though the vagus nerves play a part in regulating the depth of respiration. If the tension within the lungs is not uniform as in the case of hyperinflated bullous lesions it is conceivable that nervous influences from this portion of lung under the greatest tension could act as a governor and limit the depth of respiration and thus cause dyspnea. Allison has reported 2 cases in which he carried out phrenic nerve interruption, reasoning that the procedure would tend to reduce inflation of the cystic lesion and hence minimize the nervous limitation of the depth of respiration. One patient was relieved of his dyspnea for four months. The dyspnea returned with the return of diaphragmatic motion and was again relieved when the phrenic nerve on the involved side was permanently interrupted. In a second case the vital capacity was 1,700 ml before phrenic nerve interruption and 2,600 ml after interruption, and the dyspnea was relieved. Head<sup>13</sup> has treated some bullous lesions of the lung by Manaldi suction. We have not had experience with this method.

The following cases represent examples of emphysematous blebs and bullae and the various surgical procedures that were used in their treatment.



*Figure 1 a* Complete collapse of the left lung with tension pneumothorax on the left and mediastinal hernia — *Figure 1 b* Blunt needle in left thoracic cavity connected to continuous suction device The lung is only partially re-expanded The mediastinal hernia has been reduced about half — *Figure 1 c* Almost complete re-expansion of the lung after surgical repair of the bronchopleural fistula

## REPORT OF CASES

*Case 1* A white woman, 28 years of age, registered at the Mayo Clinic on December 30, 1947. She stated that in October, 1944 when she was four months pregnant, there had developed chills, fever and cough accompanied by rather severe pain in the region of the left costal margin. Thoracentesis had been done but no fluid was obtained. Apparently no roentgenogram had been taken. Shortly thereafter she had a miscarriage. She continued to have marked dyspnea and a dry nonproductive cough and was sent to a sanatorium. In December, 1944 roentgenograms revealed a completely collapsed left lung. The results of all studies for tuberculosis were negative. Thoracentesis had been carried out three times, resulting in partial re-expansion of the lung. No fluid was obtained. In September, 1945 and July, 1946 roentgenograms were said to show partial collapse of the left lung. In May, 1947 the dyspnea became more marked. Aspiration of air from the chest on three occasions gave temporary relief.

On examination at the clinic the patient was found to weigh only 96 pounds (about 43 kg). She was markedly dyspneic. The trachea was shifted to the right. There was marked hyperresonance over the left side of the chest. Roentgenograms revealed complete collapse of the left lung and tension pneumothorax (Fig 1a). A blunt needle was inserted into the pleural space and continuous negative pressure was instituted (Fig 1b). There was partial re-expansion of the lung. On January 6, 1948 exploratory thoracotomy was performed. The patient had a huge emphysematous bleb arising from the anterior surface of the left upper lobe. It was so large that it was attached to the diaphragm, the lateral chest wall and the apex of the chest. It had ruptured, resulting in a tension pneumothorax. In its base there were several small open bronchial fistulas. The cyst was resected and the defect in the surface of the lung was repaired. Positive pressure was applied by the anesthetist and the collapsed lung expanded readily (Fig 1c). The postoperative course was uneventful. The patient was completely relieved of her dyspnea. She was dismissed from the hospital ten days after operation.

*Case 2* An infant, five weeks of age, was registered at the clinic on August 19, 1946. The child had been born about five weeks prematurely. The pregnancy and labor had been essentially normal. From birth the child had presented a feeding problem. Breast and bottle feeding had both been attempted but had seemed to exhaust the infant. Feedings were taken slowly and were accompanied by marked dyspnea but no cyanosis or choking was noted. There had been a loss of about 1 pound (0.5 kg) since birth despite some attempts at tube feeding. On admission the infant weighed 3,000 gm. The child was markedly dyspneic even after being placed in oxygen. Roentgenograms of the thorax revealed a large emphysematous bulla on the left with marked depression of the diaphragm and a shift of the mediastinum to the right (Fig 2a). Exploratory thoracotomy was carried out as an emergency procedure. At operation the entire left side of the thorax was found to be filled by a huge bullous lesion arising from the lingula of the left upper lobe. The remainder of the lung appeared normal. The lingula was resected. The lower lobe and the remaining upper lobes then expanded normally, filling the left side of the thorax (Fig 2b). The postoperative course was complicated by the development of a small empyema which healed.



rapidly The infant was dismissed on September 28, 1946 A thoracic roentgenogram on December 11, 1946 was essentially normal The child was growing normally

*Case 3* A white man, aged 41 years, registered at the clinic on February 20, 1948 He gave a history of dyspnea on exertion for six years This dyspnea had gradually progressed and had been quite severe the past two years Three days before admission, after a bad coughing spell, he had become acutely dyspneic and was hardly able to walk Physical examination indicated complete pneumothorax on the left with some shift of the mediastinum to the right Roentgenograms confirmed this



*Figure 2 a* Large emphysematous bulla on the left which has depressed the diaphragm and pushed the mediastinum to the right—*Figure 2 b* After lingulectomy the mediastinum is in the midline, the diaphragm is in its normal position and aeration of both lungs is approximately equal



FIGURE 3

FIGURE 4

*Figure 3* Tension pneumothorax on the left with marked shift of the mediastinum to the right and mediastinal hernia—*Figure 4* Large emphysematous bulla in the upper right portion of the thorax Right middle and lower lobes are compressed

diagnosis (Fig 3) A blunt needle was inserted into the pleural space and left in place Continuous negative pressure was maintained The mediastinum shifted to the normal position and the left lung partially re-expanded The patient's dyspnea was relieved He reported that his respiration was easier than it had been for several years After forty-eight hours the needle was removed The lung promptly collapsed again Exploratory thoracotomy was advised and was performed on March 2, 1948 On exploration it was found that there were many large emphysematous blebs and bullae involving the entire lung One had ruptured and with positive pressure applied to the lung by the anesthetist the leaking bronchus could be identified Because of the almost total destruction of functioning pulmonary tissue it was necessary to perform pneumonectomy The postoperative course was uneventful The patient was dismissed in good condition three weeks after operation He reported that he had much less dyspnea than he had had before operation

*Case 4* A white man aged 41 years, registered at the clinic on March 8 1948 According to his history, a thoracic roentgenogram in 1939 had revealed the presence of pneumothorax on the right The patient had not had symptoms referable to his chest until 1944 when he noted dyspnea on exertion This gradually progressed until it had partially incapacitated him There was little cough The patient had never had asthma The results of physical examination were essentially negative The results of laboratory studies were negative except for the thoracic roentgenogram which revealed a large bulla involving the right upper lobe and markedly compressing the right lower and middle lobes (Fig 4) The results of bronchoscopy were negative On March 25, 1948 the right side of the thorax was explored The pleural space was almost completely filled with multiple large bullae The entire right upper lobe was destroyed by the lesions There were a few small superficial bullae of the right lower lobe The right lower and middle lobes were compressed by the bullous lesions Right upper lobectomy was performed The pathologist reported large emphysematous bullae of the upper lobe No bronchial communication could be demonstrated The postoperative course was satisfactory and the patient was considerably relieved of his dyspnea

*Case 5* The patient was a white woman, 38 years of age On December 26 1947 she was awakened at night with acute dyspnea She had not had wheezing or cough previously There was no pain Dyspnea on the slightest exertion continued and the next day roentgenograms revealed a tension pneumothorax on the right The dyspnea gradually improved slightly Aspiration of air on one occasion gave slight temporary relief Successive roentgenograms did not reveal any re-expansion of the lung The patient came to the clinic two months after the onset of her difficulty The lung was still completely collapsed (Fig 5a) A blunt needle was inserted and continuous negative pressure was instituted Partial re-expansion of the lung occurred (Fig 5b) but the lung collapsed again when the needle was removed The results of bronchoscopy were negative Thoracoscopy was done A bullous lesion could be seen on the surface of the upper lobe On March 10, 1948 exploratory thoracotomy was performed There were several hundred cubic centimeters of clear fluid in the pleural space The lung was encased in a fibrinous membrane which prevented complete expansion of the lower lobes There were

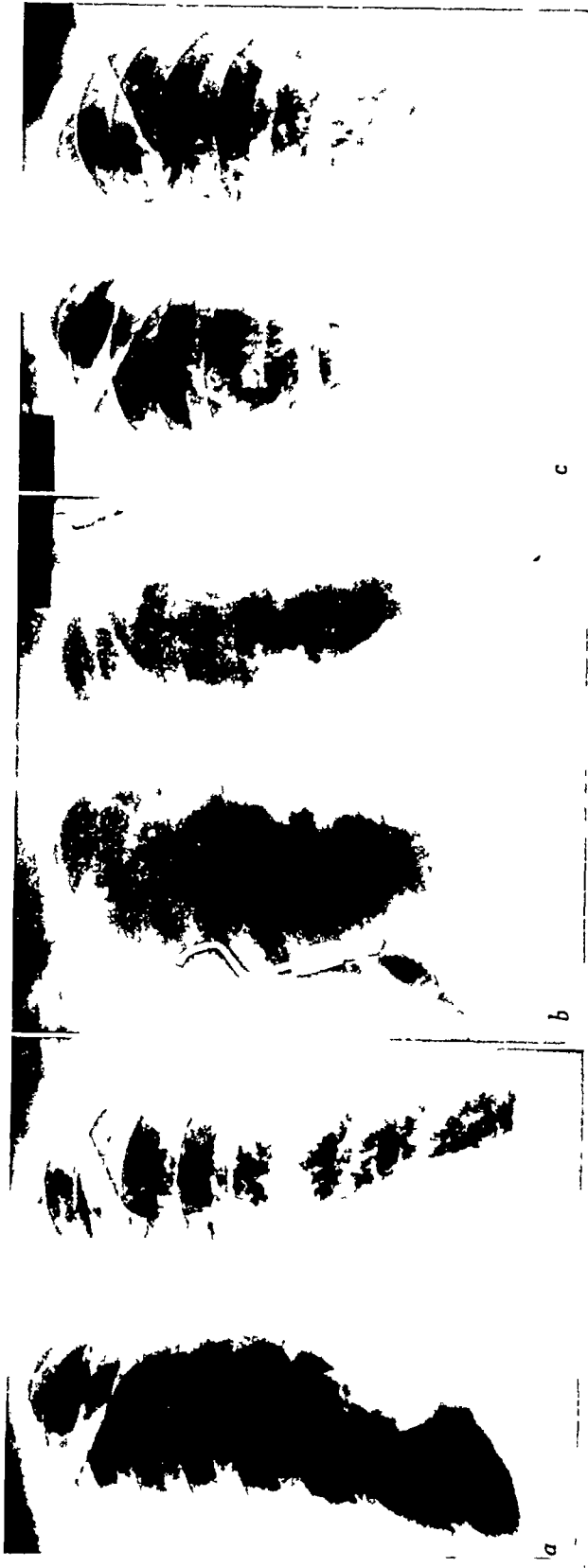


Figure 5 a Complete collapse of the right lung and some depression of the diaphragm caused by tension pneumothorax  
Figure 5 b Blunt needle in pleural space connected to continuous suction apparatus There is partial re-expansion of the lung —Figure  
5 c Appearance after right upper lobectomy and decortication of right middle and lower lobes The lung is expanded Residual pneumo-  
thorax is no longer under tension

multiple emphysematous blebs on the surface of the upper lobe. One had ruptured and there was an open bronchial fistula. The right upper lobe was resected and decortication of the right middle and lower lobes was carried out. The postoperative course was satisfactory. The remaining lobes satisfactorily filled the pleural space (Fig 5c).

### SUMMARY

The preceding cases are examples chosen from a number of similar cases that have come to my attention in recent years. As indicated, it was possible in some cases to obtain a satisfactory result by simple repair of a small surface defect, in others segmental resection, lobectomy or pneumonectomy was necessary. Before exploratory thoracotomy was performed, it was not possible in any case to determine the extent of operation that would be necessary. Since in some cases extensive pulmonary resection, even total pneumonectomy, is required, it is, of course, important to determine as accurately as possible the status of the opposite lung. The fact that these patients have been maintaining respiratory requirements with one lung, even in the presence of tension pneumothorax on the opposite side, is quite good evidence of the condition of the functioning lung. However, in some cases there may be blebs or bullae in the better lung. The most conservative surgical procedure possible should always be chosen since there is always some likelihood that the factors that have led to the development of the lesion for which operation is being performed may lead to the development of other blebs and bullae in the future. So far as we know at present this has not occurred in any of our patients as yet but the possibility must be recognized and as much functioning pulmonary tissue should be preserved as is possible under the circumstances of the individual case.

It is an interesting fact to me that these patients can have a huge air-filled cavity with bronchial communication and yet so rarely become infected. It is amazing that some of our patients have apparently gone three or four years with a complete and even a tension pneumothorax with open bronchial communication without development of a pleural infection. In some cases there may be a little clear pleural fluid, in others, none. In some instances it has been necessary to decorticate the lung before it would expand satisfactorily. In others re-expansion occurred readily when the defect was closed or the involved segment of lung was removed.

Pulmonary cysts of alveolar origin occur fairly commonly. They deserve more attention than they have received. They are not necessarily a part of a generalized pulmonary disease. They are the most frequent cause of spontaneous pneumothorax. In many instances they are amenable to corrective surgical measures with great benefit to the patient.

## RESUMEN

Los casos que se han presentado representan ejemplos seleccionados de un numero de casos semejantes que he tenido la oportunidad de observar en años recientes. Como se ha indicado, en algunos casos fue posible obtener un resultado satisfactorio con un reparo sencillo de un pequeño defecto en la superficie, en otros fue necesaria la resección segmentaria, la lobectomía o la neumonectomía. Antes de que se llevara a cabo la toracotomía exploratoria, no fue posible determinar en ningún caso lo extenso de la operación que sería necesaria. Ya que en muchos casos es necesario ejecutar una resección pulmonar extensa, aun una neumonectomía total, es importante que se determine, tan exactamente como lo sea posible, el estado del pulmón opuesto. El hecho de que estos pacientes han mantenidos los requisitos respiratorios con un solo pulmón, aun cuando ha existido un neumotórax hipertensivo en el lado opuesto, es muy buena prueba del estado del pulmón funcionante. Sin embargo, en algunos casos pueden existir ampollas o vejigas en el mejor pulmón. Por consiguiente, siempre se debe escoger el procedimiento quirúrgico más conservador que sea posible, pues siempre existe la posibilidad de que los factores que han conducido al desarrollo de la lesión por la cual se lleva a cabo la operación, puedan conducir en el futuro al desarrollo de otras ampollas y vejigas. Por lo que sepamos al presente, no ha sucedido esto todavía en ninguno de nuestros pacientes, pero débese reconocer la posibilidad y se debe conservar tanto tejido pulmonar funcionante como sea posible, dadas las circunstancias del caso individual.

Me parece a mí un hecho interesante que estos pacientes puedan tener una enorme cavidad llena de aire y con comunicación bronquial que, sin embargo, raramente se infecta. Es sorprendente que, aparentemente, algunos de nuestros pacientes han tenido un neumotórax completo, y aun hipertensivo, con una comunicación bronquial abierta por tres o cuatro años sin que resultara una infección pleural. En algunos casos puede existir una pequeña cantidad de derrame pleural claro, en otros, nada. En algunos casos ha sido necesario descortezar el pulmón para que se pudiera inflar satisfactoriamente. En otros, la reexpansión ocurrió fácilmente cuando se cerró el defecto o se extirpó el segmento pulmonar invadido.

Los quistes pulmonares de origen alveolar ocurren con bastante frecuencia y merecen más atención de la que han recibido. No son siempre parte de una enfermedad pulmonar generalizada. Son la causa más común del neumotórax espontáneo. En muchos casos responden a medidas quirúrgicas correctivas con gran beneficio para el paciente.

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## D i s c u s s i o n

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Pulmonary cysts of all types present an essentially similar problem Dr Clagett's classification of all into bronchial and alveolar cysts is practical Bronchial cysts are usually single and therefore a simpler problem Alveolar cysts are usually multiple and therefore a difficult problem for curative therapy It is only possible if the disease is to some degree localized Why some individuals develop diffuse dilatation of all or many alveoli, and others of only a few, is not clear The symptoms in either case are primarily dyspnea and gradual decrease in pulmonary function Surgical therapy of alveolar cysts is possible when the over-distended alveoli or at least the major group of them are confined to a relatively isolated part of the lung Excision of the smallest possible number which will give relief of symptoms is the ideal therapy, thus preserving as much normal function of the lung as possible At times, this may mean pneumonectomy, and at times lobectomy As often as possible the excision should be confined to a segment or even to the cyst itself, removing no normal lung tissue

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It might be worth while to mention the simple treatment resorted to in the case of a young man who had had three accidents of spontaneous pneumothorax over a spread of five years I managed the last two of these episodes When the third one occurred I continued to maintain the pneumothorax artificially for a period of three months I hoped to get sufficient pleural changes from continuing the pneumothorax to insure complete obliteration of the pleural space on re-expansion of the lung, thereby preventing any subsequent pleural accident To insure sufficient pleural stimulation I introduced on one or two occasions 10 per cent gomenol in mineral oil, each time getting a mild febrile response and a small amount of effusion After complete re-expansion had occurred x-ray inspection showed definite fogging of the pleura, suggesting that the desired obliteration of the pleural space had been attained Ten years have passed since this treatment and no other pleural accidents have occurred Perhaps the presence of the air alone, from maintaining artificial pneumothorax for the three month period, would have sufficed to produce pleural obliteration, but regardless of the degree of pleural stimulation, it seems rational to deliberately produce obliteration of the pleural sac as treatment for recurrent spontaneous pneumothorax

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RICHARD MEADE, MD, F C C P  
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I only want to rise to second completely and approve of everything that Dr Clagett has said I would like to bring out two other points He referred to the work of Dr Head and Dr Avery In those cases in which there is pronounced dyspnoea and patients are confined to bed the use of the Monaldi suction drainage will produce remarkable results In other patients who are not so crippled I would agree that by far the preferable procedure is thoracotomy to determine the exact nature of the lesion There is one more point I think worth mentioning, that is, in some of these cases in which there is a spontaneous pneumothorax of some standing, that even though you may correct the defect, the fistula may be closed, the lung will not fully re-expand because of an encasing membrane In such cases it is necessary to do a decortication If one does that, even though it may leave in the lung multiple cysts which may later rupture and, if there is a free pleural space, cause pneumothorax, after operation the lung re-expands and becomes adherent to the chest wall thereby completely obliterating the pleural space permanently

*Closing Remarks*

*O Theron Clagett, M D* I would like to thank the discussers of my paper In regard to the question of putting oil into the pleural space as an irritant and maintaining pneumothorax over a period of some time as a means of treating spontaneous pneumothorax due to blebs and bullae, I do not think it is a very satisfactory treatment Even without an irritant in the pleural space, some of these lungs that have been collapsed become covered by a fibrous film and decortication is necessary before the lung can be re-expanded, and an irritating oil would certainly result in a lung whose expansion would be prevented by fibrous reaction requiring decortication



# Tetralogy of Fallot Surgical Treatment

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Since Blalock published his first report on the surgical treatment of pulmonary stenosis, we became greatly interested in this subject

While performing an necropsy on a ten year old child who had tetralogy we found an abnormal vessel which connected the left subclavian and left pulmonary arteries (Fig 1), this vessel had a very small lumen and evidently was unable to supply enough oxygenated blood to counteract the cyanosis Nevertheless, this observation was a vivid proof that Nature, in order to overcome the disabling effects of cyanosis, used the same procedure that Taussig advocated

Last year we started to operate on cases of tetralogy having dealt, up to now, with 17 cases which are summarized in Table 1 We are aware, of course, that with this meager experience no conclusions whatsoever can be drawn, but we wish to stress some practical points which evolved from our work

At the outset we had to decide between the two operations which following Taussig's conception were developed to improve the physiologic status of these cyanotic patients Blalock's and Potts'

Blalock's technic seemed more advantageous considering the fact that if we had an accident the operation could be interrupted at any stage without any major complication, furthermore, should the follow-up of these patients show the inadequacy of the surgical ductus arteriosus to solve the abnormal physiologic situation or should well known complications of the congenital patent ductus, such as subacute bacterial endocarditis, arise we could proceed to treat these cases as we do with any patent ductus That much cannot be said of Potts' operation

To establish a sound comparison, both technics should have been performed in the same number of cases, we have not done so on account of the scarcity of Potts' clamps which were not available until very recently

Although the tetralogy of Fallot is described as a fairly standard syndrome, there are all varieties and variations of the conditions of this condition, all of which are not amenable to surgical treatment It is obvious therefore that an accurate diagnosis is an essential prerequisite to consider the surgical possibilities of a case of tetralogy

An accurate diagnosis may only be accomplished by two methods angiocardiology as described by A. Castellanos and catheterization of the heart as described by Cournand.

We have used angiocardiology routinely and have wondered why it is not widely used in the United States. Its technic is simple and may be easily mastered. It renders valuable information such as the position, size and shape of the heart chambers and great vessels (Fig. 2).

This method avoids many surgical fatalities in cases where practically all the pulmonary flow enters the lung through collaterals of the bronchial artery, which have to be divided in exposing the pulmonary artery for anastomosis. If we divide all these collaterals and there is complete absence of the pulmonary artery,

TABLE 1

Case	Age In Years	Operation	Position of Aortic Arch	Operative Approach	Dead	Alive
1	8	Blalock	Right	Left	—	+
2	3	Blalock	Right	Left	+	—
3	7	(1)	Right	Left	—	+
4	6	Blalock	Right	Left	—	+
5	9	(2)	Left	Right	—	+
6	6	Blalock	Left	Left	—	+
7	6	Blalock	Right	Left	—	+
8	10	Blalock	Right	Left	+	—
9	4.5	Blalock	Left	Left	—	+
10	3	Blalock	Left	Right	—	+
11	8	Blalock	Right	Left	—	+
12	8.7	Blalock	Left	Right	—	+
13	4	(3)	Left	Right	—	+
14	10	Blalock	Right	Left	—	+
15	11.4	Pott's	Left	Left	—	+
16		(4)			—	+
17	4	Blalock	Left	Left	—	+

(1) Ligation and section of persistent left cava superior

(2) No pulmonary artery found

(3) When the pleura was opened, the patient developed an auricular fibrillation, blood pressure fell to zero. Cardiac massage was performed. Intravenous digitals was given. Recovery ensued after half an hour. The operation was postponed.

(4) Same case as referred in No. 13, developed same complication while receiving anesthesia.

acute anoxemia develops and death ensues Blalock refers 18 fatalities following operations in which it had been impossible to find a pulmonary artery and Humphreys one If these patients had had a preoperative angiocardiology it would have shown the absence of the pulmonary artery and the operation would not have been performed

The location of the aorta may be exactly determined by angiocardiology and in some cases we have been able to measure the length of the subclavian artery

This procedure may be performed at any age, has no complications and the only warning we have to report from the surgical point of view, is to defer the operation at least a week after its performance, because it increases bronchial secretion

Catheterization of the heart is a cumbersome affair that cannot be used as a routine examination It necessitates a special team to produce satisfactory results although we must recognize that in the hands of such a team it yields invaluable information It entails some risk and fatalities have been reported It requires the joint work of a cardiologist, anesthetist, cardio-vascular surgeon, physiologist, chemist and radiologist and, at least at present, should be reserved for research centers

We have not used any particular preoperative preparation The anesthesia has been intratracheal with cyclopropane and oxygen If we have extrasystoles we change to ether To facilitate the intratracheal intubation we have not hesitated to use 1 or 2 cc of curare intravenously, without any untoward effects

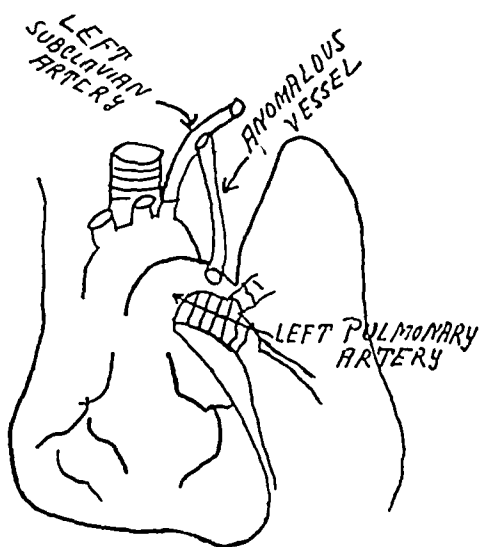


FIGURE 1



FIGURE 2

An approach through the third intercostal space, similar to that of anterior thoracotomy is used. Lately we have tried the posterolateral approach through the fourth intercostal space and find it highly satisfactory, because the dissection of both arteries, pulmonary and subclavian, is easier and the anastomosis may be performed smoothly as we have a clean access to the anterior and posterior aspects of the suture.

Blalock recommends that the incision should be made on the side opposite that on which the aorta descends. We have broken this rule in cases where the angiocardiology showed a short right subclavian. We recognize that the subclavian artery branch of the innominate provides a better angle for the anastomosis than the subclavian branch of the aortic arch, but the latter can function satisfactorily supplying enough blood to improve the cyanosis.

The exposition of the left pulmonary artery is simpler than the right. It is the highest structure of the pedicle, it runs a straight course towards the lung and can be distinctly isolated from the veins, it is the only vessel that surrounds the superior lobe on its way to the interlobar fissure. Such is not the case with the right pulmonary artery which springs up from the pedicle following an upward course and divides in two branches almost at the outset.

The vena cava should be continuously retracted in this dissection and sometimes the pulmonary veins too are in front of the artery and extreme caution must be exerted not to confuse them, as has been the case in Blalock's experience.

All these considerations led us to the thought of advocating the left side approach systematically. If we find a good subclavian which may be anastomosed to the pulmonary artery with a good angulation we perform the Blalock operation, if we do not we turn to Potts' technic. This procedure, which we followed in the last case operated on, enables us to avoid having to perform the anastomosis using the carotid artery, with its high percentage of cerebral complications.

The vagus nerve is routinely injected with 2 cc of 1 per cent novocain to avoid reflexes. In order to procure an adequate length of the subclavian artery we repeatedly have ligated the inferior thyroid, vertebral and even the internal mammary arteries, with no embolic or thrombotic complication.

The incision on the pulmonary artery is done transversely whenever it is possible, if not, we resort to the longitudinal incision.

We have not used more than 250 cc of plasma during the opera-

tion, no other infusion has been administered, from our second case on

The postoperative course has been uneventful. The two deaths reported in Table 1 correspond, one to a vago-vagal reflex during the dissection of the subclavian artery, it appears that the nerve had not been properly injected, the second fatality occurred four hours after the operation. The necropsy revealed nothing but a marked pulmonary engorgement. We feel that this baby died due to an overdose of saline solution.

Case 3 had a persistent patent left vena cava superior, which opened in the left auricle, with a coexisting tetralogy of Fallot, this anomaly was distinctly shown by the preoperative angiocardiology (Fig 3). This boy had our highest hematocrit reading 91 per cent. The performance of Blalock's operation was considered but finally we decided that the division and ligation of the left vena cava superior would reduce the amount of blood with a low level of oxygen saturation returning to the heart, with a subsequent amelioration of cyanosis.

Following the operation (Fig 4) the hematocrit reading dropped to 56, the cyanosis diminished and the well being of the patient was notably improved.

We have seen this patient two months after the operation and the contrast with his preoperative status is remarkable, especially relating to his working capacity. This boy, who hardly could walk without a fainting spell, is now able to play base ball.



FIGURE 3



FIGURE 4

## SUMMARY

Seventeen patients with tetralogy have been operated on with a mortality rate of 11.6 per cent

The value of angiocardiology is emphasized, and its use is recognized as a routine exploration. It avoids fatalities in cases where no pulmonary artery is found.

The operation of a case of persistent left vena cava superior, opening in the left auricle, is reported.

The left thoracic approach and postero-lateral incision are recommended as they give the alternative of performing either Blalock's or Potts' operation.

## SUMARIO

Se presentan diecisiete casos de Tetralogía de Fallot, operados con una mortalidad de 11.6 por ciento.

Se hace especial hincapié en el valor de la angiocardíografía, la cual se preconiza como una exploración de rutina. Su empleo evita la muerte de aquellos casos en que disecado el pedículo pulmonar, no se encuentra arteria pulmonar.

Se reportó la operación de un caso con vena cava superior izquierda, la cual desembocaba en aurícula izquierda.

Se recomienda el acceso por hemitorax izquierdo, así como la incisión posterolateral, ya que de este modo si no se puede practicar la operación de Blalock, se hace la de Potts.

*Addendum* Since this paper was written, 11 additional patients have been operated on with one fatality, which yields a mortality percentage, considering the whole group, of 10.7 per cent.

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# The Importance of Various Mechanical and Circulatory Postoperative Pulmonary Complications

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Pulmonary diseases constitute some of the most feared complications in the practice of the general and thoracic surgeon. They have been stated to occur in 2 to 4 per cent of all surgical patients and in 10 per cent of all abdominal operations. Moreover, of all surgical patients it is said that 0.6 per cent will die of some pulmonary malady. Since the advent of the chemotherapeutic and antibacterial drugs, the incidence would seem to be less, but their occurrence is still of sufficient gravity to warrant discussion.

The majority of pulmonary hazards can be conveniently classified under three headings: mechanical, infectious, and circulatory. All such disorders begin as any one of the three, but due to the intimate relationship of the pulmonary broncho-vascular structure and lymphatic lung network, a complexity of affliction may result. For instance, pulmonary infarction may easily be found the forerunner of pneumonia, abscess may lead to atelectasis, also, atelectasis may be seen to accompany either the infectious or circulatory diseases.

Although the most prevalent postoperative pulmonary complication would seem to be bronchopneumonia, we are less concerned with its appearance than we are with the more basic phenomena which predispose to it. A goodly number of these cases can be ascribed to invasion of a virulent organism in a host of lowered resistance. Naturally, many infectious processes seen postoperatively have their origin in an unrecognized inflammatory disease that was present preoperatively. This may be evidenced by simple nasopharyngitis, sinusitis, or bronchitis. Other chronic pulmonary infections as bronchiectasis and lung abscess have been ascribed as causative factors of seemingly acute postoperative complications.

We should like to recall three theories which have been proposed in the past to explain the onset of pneumonitis postoperatively: namely, (1) Whipple's theory of aspiration pneumonia, (2) the theory of infected emboli proposed by Lichtenburg, Cutler, and others, and (3) Coryllos' contribution on atelectasis. Although the first two were well founded, an overwhelming amount of material

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has favored Coryllos' theory. He showed that there were pneumococci present in 72 per cent of the tracheae of all operated patients but that these organisms were present 100 per cent of the time in those patients who developed atelectasis. The secretions harboring pneumococci were found to be more viscid and therefore more difficult to eliminate than ordinary bronchial secretion. The further work of Cooper and his associates in differentiation of these pneumococci showed every conceivable type present.

### *Atelectasis*

The most important clinical entity as a mechanical factor is atelectasis. Its seriousness is convincingly shown in the report of Christopher and Shaffer who found upper respiratory disease prevalent in 30 per cent more patients with it than without it.

What are the causes of atelectasis? Experimentally, it has been produced in a number of ways. After the work of Faulkner and Faulkner on mucus plugs, Lee, Tucker and Clerf reproduced it in dogs by inserting such plugs into one stem bronchus with the aid of a bronchoscope. The most significant finding was an absorption of air beyond the point of obstruction producing collapse of the alveoli. Galbraith and Steinberg, on the other hand, produced atelectasis without first producing bronchial obstruction. Approaching it from an entirely different angle, Scott and Ivy postulated a nervous reflex which causes venous engorgement in the lung, coincidental with a bronchiolar spasm. In still another contribution, histamine was stressed as a factor in the production of atelectasis. This substance, although present in large amounts in normal lung tissue was not found by Lindskog to be eliminated by fixation and storage in the lung but "probably by the hydrolytic action of histaminase in blood and tissues." Although histamine can produce bronchiolar constriction, it would seem to account for very few, if any, of the usual run of cases seen post-operatively. While the importance of pulmonary stasis and nervous reflexes is granted, we believe the greatest importance lies in the mechanical plugging of the bronchi with mucus, since elimination of this factor with the bronchoscope usually results in prompt aeration of the affected segments of the lung.

This brings us to a consideration of some of the causes of atelectasis in surgical patients.

- 1) **Bronchial occlusion.** We refer to the presence of known or unrecognized intrabronchial and extrabronchial diseases which may materially narrow the lumen of the bronchus. This may constitute mucus plugs, tumors, foreign bodies, stenosis, granulations, enlarged lymph nodes, effusions, aneurysms, abscesses, or virtually any inflammatory process producing sufficient edema



to compress or reduce the caliber of the bronchus. The most frequent of these in postoperative patients is the mucus plug. Blood in the bronchi was found to be a pertinent cause of atelectasis in 79 per cent of the tonsillectomies analyzed by Myerson. Asthma with its bronchial narrowing was found to be a background in 10 per cent of all postoperative atelectasis.

2) Inability of the patient to cough. After anesthesia has been administered, patients who do not raise accumulated secretions from the bronchi may be unable to do so for many reasons.

(a) Coma. This might concern excessive preoperative medication, cerebral accidents, diabetic coma, or the depth and duration of the anesthetic itself. In a remarkable study of 7874 operations at the Wisconsin General Hospital, Rovestine and Taylor found that those lasting 1 hour or less had from 50 to 100 per cent fewer pulmonary complications than those lasting from 1 to 1½ hours. As the duration of the anesthesia increased, the morbidity also increased to the point wherein those lasting 2 hours had three times the number of complications while those lasting over 3 hours showed 31 per cent with some pulmonary complication.

(b) Type of anesthesia. It is not necessary to have a loss of consciousness in anesthesia to reduce the cough mechanism. Many reports cite a higher incidence of atelectasis from spinal anesthesia than from general anesthesia. One of the factors thus responsible is the paralysis of the lower intercostal muscles that this agent produces. Inhalation agents on the other hand produce certain irritating effects on the bronchi when used over a long period of time which are not present with the injection agents.

(c) Severe postoperative pain. Patients who suffer intense abdominal or thoracic pain are not willing to cough. Upper abdominal incisions are more painful than lower abdominal incisions. In King's study, laparotomies and hernias produced 14.3 per cent pulmonary complications as compared to 1.2 per cent in all other surgery. In this connection, wounds that heal per primum produce fewer lung complications. King thus found that clean appendectomies were followed by pulmonary complications in only 7.1 per cent, while infected cases with drainage had a pulmonary morbidity of 27.9 per cent.

(d) Position during surgery. This concerns the degree of inclination of the thorax during and after the operation. If secretions are present, the head-down position is more apt to keep bronchial secretions drained than any other position. Gray noted that he could reduce postoperative atelectasis by as much as 30 per cent when the Trendelenburg attitude was maintained during the operation and for the next 24 hours thereafter.

(e) Miscellaneous causes. Ineffective cough may be the result of insufficient strength. Patients who are poor surgical risks fre-

quently lack the vitality for an adequate cough reflex. This conforms to Henderson's belief that hypoventilation of the areas of the lung was due to a general reduction in muscle tone and subsequent diminution in tidal volume. Tight abdominal binders have been known to hinder the cough mechanism particularly in the lower lung fields. Paradoxical respiration as seen in thoracic injuries and operations may disturb the stability of the thorax so that cough is ineffectual. The administration of heavy doses of atropine and/or maintaining the patient in negative fluid balance may thicken bronchial secretions sufficiently to prevent their expulsion. Patients who are chronic smokers are apt to have tenaceous mucus. Included in this category are those cases of bronchiectasis who are unable to empty their bronchi completely of mucus.

3) Location of the incision. Upper abdominal incisions favor limitation of the lower half of the thorax and may contribute in this way to a higher percentage of atelectasis. Pasteur laid emphasis on the rise of the diaphragm, and more recently Overholt and Veal have recalled its importance. In this connection, the diaphragm was found to be elevated in 93 per cent of patients undergoing abdominal surgery. Significantly enough, Churchill and McNeil noted that its elevation reduced vital capacity some 30 to 50 per cent.

4) Operative trauma. An abdominal reflex was described by Goltz and again by Scott and Ivy which results in a viscerocardiac inhibition. When these investigators tapped on the abdominal organs of animals or pulled on the viscera, there was a definite stasis of general and pulmonary circulation and a coexistent bradycardia. This was often accompanied by temporary apnea. These latter two factors were all that Galbraith and Steinberg had found necessary to produce atelectasis experimentally.

What are the clinical features of atelectasis and how can it be recognized? When our attention is called to such a patient, it may be for either an elevated temperature, tachycardia, dyspnea or cyanosis. A combination of these symptoms and findings may frequently exist. These patients are listless and are unwilling to move, even in the bed. If they are conscious, as most of them are, they act as though they were afraid to move. They frequently have pain particularly at the operative site. Some have chest pain. This pain plays a dominant role in their immobility and feeble effort to cough. If they do cough, it is weak and ineffectual. In our experience, patients who cough effectively and unhesitatingly rarely develop atelectasis.

Physical signs are present some time before roentgen findings are demonstrable. Cyanosis and dyspnea are prominent and there

is a noticeable limitation of motion of the portion of the chest affected. Temperature and pulse are usually elevated conspicuously over expected postoperative levels. The percussion note may be dull if the process is localized. The early stages in the dry form may show only diminished breath sounds, but after secretions have been dammed back for some time, rhonchi may be audible without the aid of the stethoscope. The retained mucus may be heard as high as the stem bronchus or trachea and may be found more easily by rotating the patient on the uninvolved side. Mediastinal shift to the side of collapse may often be demonstrated by palpating the cardiac apex impulse. Occasionally, the act of turning the patient in this way will promote drainage and ventilation to the hypofunctioning lung and literally clear the process while one is attempting to make the diagnosis.

Little need be said about the roentgen diagnosis of atelectasis. Films may present findings of either a patchy or massive process. The former finding may be fairly diffuse after the condition has existed for a time when secretions have been forced into other parts of the lung. Not infrequently the demarcation between atelectasis and a pneumonic process is ill-defined. Attention is called to the oft-missed retrocardiac type which may require special views for demonstration.

If the preceding observations are significant, then a certain regimen can be set forth which will materially lower the probability of occurrence of atelectasis. If such a complication does occur, it can best be managed during its formative stage.

Preoperative roentgenograms should always be taken. Pulmonary disease is better diagnosed by the use of the x-ray before complications have developed. In most institutions these films are routine practice and frequently denote pulmonary disease when the clinician is unable to detect it by physical signs. It is also advisable to complete whatever diagnostic studies are indicated by unexplained roentgen shadows. We refer particularly to the use of bronchograms and the bronchoscope for the clarification of suspected intrabronchial changes.

In the preoperative preparation of the patient we are chiefly concerned in sending him to surgery with as normal a respiratory apparatus as possible. Naturally, operation in any patient with evidences of upper respiratory infection is postponed until such a process clears. Unless uncontrollable, it is likewise best to postpone operation in patients who have hemoptysis until this symptom abates. In bronchiectatic patients, as well as chronic smokers, postural drainage is emphasized to clear the bronchi of all secretions possible. Ammonium chloride a day or two before surgery often enhances the elimination of viscid secretions by

promoting liquefaction. Some patients are given prophylactic antibiotic or chemotherapeutic medication for 24 to 48 hours before operation. Although statistics are not readily available, we believe the use of these drugs has "paid off" in preventing a certain proportion of pulmonary complications.

In the operating room we concern ourselves chiefly with the depth of narcosis. Excessive preoperative medication is condemned and atropine is never ordered unless for definitive reasons. The anesthesia is selected to meet the needs of the surgeon without increasing the operative risk. Some operators, in order to obviate prolonged anesthesia, delay induction until the operative site has been prepared and the field sheets placed. The patient may be placed in Trendelenburg's position to facilitate drainage of bronchial secretions. When the lateral recumbent position is necessary, as in renal or thoracic surgery, the head-down position can be attained just as easily as when the patient is in the dorsal position. The only contraindication to Trendelenburg's position would appear to be in cases of abdominal suppurative processes where dependent drainage toward the iliac fossa is desired. However, this may be a point for conjecture. During the operation the care of the tracheobronchial tree is in the hands of the anesthetist. Needless to say, a well-trained individual will make every effort to keep secretions free by frequent use of the aspirator, with or without an endotracheal tube. The avoidance of excess secretions can be frequently managed by careful selection and use of various inhalation agents. It would appear to us that expert anesthesiologists have less difficulty with excessive secretion formation than a less qualified technician.

After operation, tight adhesive strapping is avoided and the lower thorax is never incorporated tightly in the dressings. The anesthetist should routinely arouse the patient by the use of 10 per cent carbon dioxide in oxygen. This promotes hyperventilation of all segments of the lung and tends to loosen mucus plugs from the bronchial apparatus. It is also beneficial in arousing patients to a state of consciousness where they can cough forcibly. We always demand that the patient cough before leaving the operating theater. Trendelenburg's position is maintained until the patient reacts sufficiently. After this time, frequent change of position is recommended even to a semi-Fowler's position where some patients expectorate more effectively. Patients who cannot be aroused promptly, e.g. under ether narcosis, may be subjected to bronchoscopy. This is particularly true after thoracic operations.

Postoperatively, patients are encouraged to cough periodically every 3 hours for the first few days. If they are unable to do so, we again resort to carbon dioxide inhalations. If mucus still per-

sists, we next resort to a change of position, older writers spoke of this in the prevention of "hypostatic pneumonia." By turning the patient alternately on the uninvolved side for 30 minutes then 15 minutes on the involved side, we can help to promote drainage from the uppermost lung and obviate pulmonary venous stasis. Not infrequently, patients are aided to a sitting position to effect this change. If this is not entirely effective or if signs of atelectasis become evident, we next suggest the use of intratracheal suction as described by Haight. This is a valuable manœuvre that should be known by every postoperative team. It is repeated every 4 to 6 hours until the cough reflex becomes well established. Very frequently, tracheal aspiration can be begun in the operating room if an endotracheal tube is in place. The anesthetist merely inserts a small rubber catheter attached to the suction machine. There are times however when one must resort to bronchoscopy to remove mucus out of reach of the catheter and we do not hesitate to have a unit at the bedside in readiness when the patient develops signs of impending atelectasis. We feel that its use has aborted an otherwise certain bronchopneumonia in many instances. The use of steam inhalations is of definite value in thinning secretions sufficiently that the patient can expel them. Ephedrine at times is also helpful in enlarging the bronchial lumen when a certain degree of spasm or edema exists. We also recommend the use of multiple intercostal block as advocated by Bartlett and others for the control of thoracic pain and thereby facilitate cough.

Most thoracic patients are routinely placed on penicillin therapy postoperatively. In the event of atelectasis the dosage of this agent is increased to conform to therapeutic standards. Then again, one may employ streptomycin or one of the chemotherapeutic drugs depending on the type of organism found in the sputum. It has been definitely shown that the effective time to use these drugs is early in the disease and we employ them to the fullest extent in threatened pneumonic cases.

The following case illustrates some of the points previously outlined, even though the patient was handled long before we were fully aware of all the factors responsible for postoperative pulmonary disease.

Mrs. F.B., a white female, age 31, was already under hospital care for tuberculous peritonitis with ascites. She had been in the hospital some 27 days when on May 4, 1936 she suddenly developed signs of intestinal obstruction. After meager preoperative preparation including 1000 cc of intravenous fluid, she was subjected to exploratory laparotomy under spinal procaine (150 mg) anesthesia. The operation was carried out in the head-down position and no supplementary anesthesia was used. The operator found diffuse inflammation of the entire peritoneum with

thickened plastic exudate surrounding the adnexae and small intestine. This was most pronounced in the area of the cecum and ascending colon where the adhesive process appeared to be producing more obstruction than at other portions of the bowel. A cecostomy was performed and a few adhesions liberated, but it did not appear that this would be too successful in freeing much of the obstruction. The outlook was considered hopeless and the abdomen closed in routine fashion. Her postoperative course was complicated by a temperature rise to 103 degrees F within 24 hours. The respiratory rate was 30 and the radial pulse 130. One could hear only distant breath sounds in the lower portions of both lungs accompanied by frequent harsh rales. She refused to cough effectively. Ten per cent carbon dioxide in oxygen was administered without apparent benefit. Unhesitatingly, she was subjected to bronchoscopy and large amounts of thick tenaceous mucopurulent secretion removed from both lower lobe bronchi. A roentgenogram of the chest then showed a patchy atelectasis in both lung bases but the lung was fairly well aerated. Following bronchoscopy, breath sounds were heard equally well in all portions of the chest with only an occasional rale, and within 24 hours the temperature was 99.4 degrees F and the respiratory rate 22. Thereafter, she was able to cough effectively and this was encouraged at repeated intervals of 4 hours until the 5th postoperative day. At this time she was afebrile and aside from a slow convalescence from complete obstruction and supplemental parenteral fluids for some 19 days she made an excellent recovery. Check-up roentgenogram of the chest after 21 days showed normal clearing in all portions of the lung. She remained in the hospital 92 days after operation still convalescent from tuberculous peritonitis.

We feel that aside from the grave situation in the abdomen of this patient, her complication of atelectasis would have surely resulted in bronchopneumonia from which she could not have recovered. We credited a prompt bronchoscopy to correction of this otherwise unavoidably fatal complication.

An additional case is presented to illustrate further the prophylactic care instituted against atelectasis, and the shortcomings of such a preventive regimen in the occasional case.

Mrs. R.B., a white female, age 21 had a 6 months' history of cough and loss of 8 pounds in weight. There was no hemoptysis. The family history revealed no tuberculous contacts or deaths. Her past history portrayed a pneumonia in infancy and no other serious illness. Her menstrual history was normal. Examination revealed a thin young adult female who was 62 inches tall and weighed 89 pounds. The radial pulse was 90 and the blood pressure 136/90 in the right arm. Physical findings were abnormal only in the examination of the chest. Occasional rales were heard anteriorly and posteriorly over the right apex. Laboratory findings were significant only in the finding of acid-fast bacilli in the sputum. The roentgenogram of the chest taken on the day of admission (November 15, 1946) showed a 4½ centimeter cavity in the right upper lung extending down to the 5th interspace posteriorly. Except for a small surrounding zone of inflammation, other portions of the lungs were within normal limits.

A trial of pneumothorax was ineffective. She was subjected to bron-

choscopy in anticipation of thoracoplasty, to rule out tracheobronchial tuberculosis. The findings were normal. On January 11, 1947, under cyclopropane-oxygen anesthesia and in slight Trendelenburg position, a 2½ rib right thoracoplasty was performed. The operation proceeded in a normal fashion and without significant departure in the blood pressure or respiratory graphs. After the patient was turned to the dorsal position, she showed signs of moderate cyanosis and one could hear rhonchi in the region of the trachea. Inasmuch as an endotracheal tube was not in place, she was bronchoscoped at once, and a moderate amount of mucopus removed from the trachea and both stem bronchi. Breath sounds then appeared fairly normal and she appeared to be ventilating the left lung adequately. The first 18 hours postoperatively were uneventful but she then began again to show cyanosis, dyspnea, an elevated pulse to 130 and a temperature of 102.2 degrees F orally. Auscultation revealed distant breath sounds over the entire left lung. Cough was feeble and unproductive. A roentgenogram revealed complete atelectasis of the left lung with moderate shift of the trachea to the left. The only ventilating portion of the lung was in the lower right chest. Oxygen was administered by BLB mask to relieve cyanosis and she was subjected to intratracheal suction. This was effective in raising a few thick plugs of mucus after which one could hear breath sounds much clearer in the left lung. She was unable to breathe in any but semi-Fowler's position and the routine of change of position was abandoned. Temperature continued to rise to 105 degrees F but the pulse remained at 130. She seemed to be breathing comfortably and continued to cough effectively. Sputum culture at this time revealed many pneumococci and the postoperative dose of penicillin was increased to 40,000 units every 3 hours. By the 4th postoperative day, the temperature suddenly fell to normal and the oxygen was discontinued. Penicillin was continued for 3 more days. A check-up roentgenogram on the 7th day revealed nearly complete clearing of the entire left lung and she was transferred to her sanatorium on the 10th postoperative day. She went through her succeeding two stages of thoracoplasty without event and eventually was discharged from the sanatorium with sputum cultures negative for acid-fast bacilli. The roentgenogram showed evidence of cavity closure and the left lung remained clear of any pathology.

This is a case of diffuse lobar pneumonia which was initiated by atelectasis of the left lung. This complication developed in spite of the bronchoscopic intervention to avoid it, but we believe that the patient withstood her pneumonia with a brighter outlook than if we had not enforced such detail in her postoperative care. One might theorize that she was developing an upper respiratory infection at the time of surgery but we believe that bronchial obstruction from the mucopus was a more likely cause.

#### *Spontaneous Pneumothorax*

Of not occasional interest is the occurrence of pneumothorax in operative and postoperative cases. The causes of pneumothorax may at times be quite certain as in various forms of pulmonary disease, but at other times one may be quite at a loss to find any

definite etiologic reason. Of the many thoracic conditions which may produce this complication, tuberculosis leads. Certain cancerous lesions of the pleural surface of the lung, cystic disease, or any inflammatory process near the pleura may harbor the underlying lesion. The mechanism of the aforementioned diseases is usually by tear of an adhesion which also tears the lung, allowing air to enter the pleural cavity. Blebs on the surface of the lung have been known to rupture spontaneously without adhesion formation. Reports have reached the literature wherein excessive positive pressure with anesthetic machines caused rupture of the lung, trachea or bronchi with resultant pneumothorax. Phillips reported one such case occurring bilaterally. Stephens noted 3 cases of pneumothorax in thoracic operations occurring on the contralateral side. The mechanism here was undoubtedly one of tearing the mediastinal pleura during dissection. Any operation in which an attack is made on the pleura, either purposefully or inadvertently, may result in pneumothorax. Special mention is made of nephrectomy and lumbar sympathectomy where the lower border of the pleura may not be clearly seen. This complication has even been reported following bronchoscopy.

The onset is usually quite sudden and dramatic. If the patient is awake, there is usually a severe stabbing pain on the affected side of the thorax. This is followed shortly by dyspnea of a varying degree. If a valvular action results from the tear in the lung, the air may continue to fill the thorax and compress the lung. A splinting action of the abdominal muscles may accompany such a process, and acute intra-abdominal disorders have often been mistakenly diagnosed. Rolleston almost subjected a patient to laparotomy for ruptured peptic ulcer with this condition. Dyspnea may be more marked when the patient lies on the uninvolved side, but most patients prefer to remain in a sitting position.

The diagnosis is quite obvious if one's attention is focused on the thorax. Respiratory motion on the involved side is usually greatly decreased and may even be paradoxical. On percussion, the note is tympanic and auscultation reveals absent breath sounds. The cardiac impulse will be shifted to the side opposite the pneumothorax, and in some cases of left-sided involvement, the heart may lie entirely within the right thorax. The unaffected lung is frequently crowded within its own side of the thorax and one may even see abdominal distention from the displacement of the diaphragm downward.

If dyspnea is marked, one should not wait to confirm findings with the roentgenogram as the process may end fatally in a short time. Without taking time for anesthesia, one should thrust a moderate-gauged needle (17-19) of at least 2 inch length through



one of the accessible interspaces of the involved side even though a syringe or manometer is not available. Where the latter is accessible, one can measure with some degree of accuracy the amount of air withdrawn, together with the pressure within the thorax. Such pressures will read anywhere from neutral to highly positive until pressure is relieved. If a manometer is not at hand, air should be allowed to rush out the needle until the cardiac apex impulse returns to its normal position. Using the pulse as a guide, one can slow the shift of the mediastinum so that circulatory embarrassment does not follow. Too rapid a shift of mediastinal contents will lead to greater tachycardia and eventual cardiovascular collapse. The patient, if awake, feels relieved from the moment the needle enters the thorax. One can then remove the needle and check the position of thoracic organs with a roentgenogram. Repeated withdrawals may be necessary where the fistula is still present. If pneumothorax recurs within a few hours, one may feel safer to leave a blunt-ended needle indwelling within the pleural cavity, connecting the hub of the needle to rubber tubing whose free end is placed under a water trap. An occasional case will require open thoracotomy to close the fistula, but as a rule, most will reexpand fully after a limited number of days or weeks. Stubborn pneumothoraces which do not reexpand readily will frequently form a moderate effusion. This should likewise be aspirated and the pleura kept fairly dry.

The following illustrative case is a fairly common one in the practice of the thoracic surgeon, although most do not end fatally as this one did.

A white male, age 21, was under treatment for a simultaneous left empyema and abscess of the right middle lobe. The previous history was one of upper respiratory infection which did not respond to treatment but resulted in empyema within a few days. This was drained surgically and his condition improved, only to relapse after 7 weeks. Bronchoscopy and transfusions seemed to improve him clinically, but the abscess grew steadily larger and surgical drainage was decided upon. Under local anesthesia the parietal pleura overlying the abscess was exposed with resection of short segments of two ribs. The pleura was packed with gauze due to inefficient symphysis and the wound left open. Suddenly, after 2 hours, he developed marked dyspnea and unconsciousness from which he never recovered, dying within 3 hours. Continuous withdrawal of air from the right pneumothorax and an oxygen tent failed to save him. We attributed death to cardiovascular collapse due to his prolonged illness and augmented by the mediastinal shift. Post-mortem exposure of the operative site revealed a spontaneous tear in the pleura, but no projecting rib stump to account for it.

#### *Pulmonary Embolism*

In postoperative complications, circulatory phenomena play a much different role. Most of them occur in the form of emboli

or infarcts under most puzzling circumstances. Heretofore, we have regarded these complications occurring in seemingly normal patients. The postoperative convalescence for the first few days had been uneventful and without incident. Suddenly without apparent warning, patients developed marked dyspnea, pallor or cyanosis, and signs of profound shock. Death came in a matter of a few minutes to a few hours. Occasionally one would survive but not without a stormy course. Every surgeon has probably witnessed this catastrophe and has been at a loss to explain it to the relatives, let alone to himself. Our supposition that these patients were progressing normally, was, of course, erroneous.

In the first place, these people appear to be constitutionally different than others, they are phlegmatic, may be obese, can be young adults but are more often in advanced age groups, and may run a relatively slow pulse. The latter finding is not too constant, however. Rehn would stress that they are the cachectic type who are chronically ill and are in the upper age brackets. We recognize that patients in the middle or old-age bracket are more prone to develop embolism, but when a young adult becomes the victim, we are impressed no end. Secondly, some of these people have various unrecognized pathological processes which are precursors to embolism. There may be cardiac vegetation, saccular aneurysms or arteriovenous shunts of varying size, or some element of cardiac peripheral decompensation producing venous stasis. They may have seemingly innocuous lesions where thrombi arise, as varicosities of the lower extremity, broad ligament, or prostatic plexus. Evidence of phlebitis may or may not be present or have ever occurred. Rehn refers to the presence of infection, deficiency of liver glycogen, decreased alkali reserve, and circulatory liability as evidenced by control tests. An imbalance of the sympathetic nervous system or possible hormonal imbalance would seem to be one of the responsible factors. Although females are more susceptible than males (3/2), males are more frequent victims of fatal emboli. Barker and his associates found that the occurrence of embolism in blood disorders was 93 per cent while those with no predisposing element was only 19 per cent. Other diseases in a similar tabulation were significant, embolism occurred in cardiacs in 72 per cent, peripheral vein disorders in 56 per cent, cancer patients in 47 per cent, and severe infections in 58 per cent. It is also significant that the rate in obesity was higher, patients weighing over 200 pounds had a susceptibility of 71 per cent, while those under 200 pounds developed it in 32 per cent.

The third and most significant feature of these cases is that many of them show none of the previous tendencies, and throm-

basis occurs in apparently healthy subjects. The chief offender in such an individual is venous stasis, brought about by post-operative immobility. One cannot say that the magnitude of operation with impending shock or collapse had anything to do with its predisposition. One is impressed when such a patient succumbs of embolism after a relatively non-shocking and less major appendectomy or hernia repair. The site of the thrombus in such individuals is usually found in the deep popliteal or femoral veins. Homans has shown that autopsies revealed thrombosis in these deep calf veins in over 50 per cent of the cases. These individuals are unwilling to move about during their first days of convalescence. Immobility seems manifest particularly in the lower extremities. About the 7th day or so, when they do arise and move, a weakly organized thrombus is freed, or its projecting free end breaks into the circulation. The circulating thrombus is thus destined to lodge in the pulmonary vascular system. Occasionally, one finds that the thrombus arises from the region of the operative wound, but this is not the rule. Where normal healing involves organization of thrombi in ligated vessels, these individuals for some reason produce propagating thrombi which break easily. If the embolism is small, and vagal impulses are not too severe, infarction of a segment of lung results, with possible eventual recovery. Some patients are subjected to repeated showers of such emboli, and when they appear to have recovered from one episode, another possibly more severe strikes them. If the embolus is large or extensive, it may block a large portion of the pulmonary circulation and a rapid exitus results. There is no significant alteration in the coagulability of the blood in these patients despite reports to the contrary. Although some investigators have found significant alteration in the prothrombin levels of the blood, many show no such abnormality. There is merely a venous stasis, and if there is any other pathognomonic finding in the blood, it does not show by current diagnostic methods.

The basis of sudden death in these cases has been brought out by the experimental work of deTakats and his associates who reproduced embolism in dogs with injections of starch emulsion. Depending on the amount and consistency of the emulsion, two types of embolism were apparent, both comparable to clinical types: (1) massive embolism resulting in death, and (2) precapillary embolism from which the dog might recover if large amounts of emulsion were not used. Typical electrocardiographic tracings resulted from both types in many of the animals, and if the embolus was not too extensive, the dogs could frequently be saved by the use of oxygen and the vagus-blocking drugs (atropine).

The effectiveness of the latter derivatives lay in the former experimental findings of increased pulmonary artery pressure and isolation of receptor fibres by Takino and Watanabe in the adventitia of this vessel. Hypertonus of the vessel elicited excessive stimuli to these fibres which gave typical vagal responses. The terminal effects were cardiac standstill and ventricular fibrillation with a shift of the pacemaker to the A-V node. Such findings are similar to those obtained by coronary occlusion, in fact, there was evidence of decreased blood flow in the right coronary in many of the animals.

An alert surgeon will diagnose this condition long before embolism occurs. Subjectively, complaints are minimal but present. There is vague leg pain accompanied by tenderness in the outer posterior aspect of the calf. Objectively, there is pain in the calf on dorsiflexion of the foot (Homans test) and there may be local tenderness over the femoral triangle. Likewise, mild cyanosis and edema of the foot may be manifest when the member is in the hanging position. Such a calf is usually firmer and feels more unrelaxed than the corresponding normal leg. The calf should be measured frequently to denote changes in inequality. Pulse rate and temperature are higher than expected postoperative levels. In many cases a temperature of only 99° or more has put us on our guard to search for more concrete evidence. If the patient has already experienced pleural pain, dyspnea, cyanosis and possibly hemoptysis, our diagnostic eye is still turned to the lower extremities where the process has likely started. One can corroborate clinical pulmonary embolism with the x-ray and electrocardiogram but confusion may result if the findings are not typical. We wish to emphasize that the diagnosis of leg thrombosis should be made before pulmonary complications ensue. Often too frequently, when lung embolism awakens our interest, it is too late. Robertson showed that out of 149 cases of severe embolism, 39 per cent died within one hour. Many other series present similar figures. The diagnosis of embolism is not always simple as Nygaard has shown. In a study of 289 cases coming to autopsy at the Mayo Clinic, a correct diagnosis was made in 82.35 per cent. Other diagnoses made were coronary occlusion, indeterminate causes, shock and hemorrhage, peritonitis, pulmonary edema, and cerebrovascular accidents. The rationale of such diagnoses can be easily seen.

Since therapy is almost at a loss in handling this complication in its most serious phase, expectant treatment and prophylaxis is all we can offer these individuals. As stated before, a large percentage of these patients die immediately or within a few minutes. The reader is referred to the reports of deTakats and

Nygaard for further statistics. We doubt that the Trendelenburg operation of removal of the clot from the pulmonary artery will ever have a place in any but the occasional case. One wonders in these successful cases whether the patient might not have recovered spontaneously. Nygaard has gone into the impracticability of embolectomy, even in large institutions. Much, however, can be done to prevent this tragedy.

First of all we must become conscious of those patients in whom we feel there is a constitutional background for embolism. This is difficult and rather empirical but a careful history and examination will give significant data in many cases. Emphasis is placed on the presence of varicosities and chronic illness, particularly if there has been a past history of infarction. Next and most important of all we concern ourselves with those patients who do not move freely after their surgery. Any alteration in the pulse or temperature should make us turn our interest to the leg veins for further evidence of impending thrombosis.

Prophylactically there are many things that one can do. Walters advocated thyroid extract daily to promote tachycardia but control figures were not too impressive. We believe that the most effective preventive measure is early ambulation. If this is not possible, one should at least enforce leg exercises. These may be started as soon as the patient reacts from anesthesia. Motion is also encouraged in the head, arms, and hips as well. The patient should be able to turn himself within 12 hours or sooner. He is frequently assisted to the sitting position without the back rest on the 1st postoperative day and may begin to sit on the edge of the bed by the 2nd day. Ambulation then begins anywhere from the 1st to the 4th postoperative day. In major thoracic operations patients are usually out of bed on the 3rd or 4th day. Statistics would indicate that early ambulation has not had a deleterious effect on wound healing.

If femoral thrombosis develops despite prophylaxis, we may still prevent embolism from occurring. The pendulum of therapy changes abruptly from one of activity now to complete rest to the thrombosed part. Every effort is made to keep the thrombus from dislodging. The leg is elevated to allay venous stasis and efforts are made to incite phlebitis. Heat from a hot water bag or cradle are somewhat effective. Since the advent of the anticoagulants, we have supplementary drugs which can do much. Many operators use heparin and dicumarol prophylactically before thrombosis occurs. Murray and Best cite the use of heparin in 315 patients postoperatively without a single incidence of embolism, while their control series developed this complication in from 22 to 75 per cent. Again Rehn used anticoagulant therapy

with somewhat stricter indications in a group of 1596 patients Only 5 (0.32 per cent) developed thrombosis and 1 case embolism (0.15 per cent) The latter case was fatal In the control group of 1369 where only general preventive measures were used, 26 (2 per cent) developed thrombosis, 17 (1.24 per cent) developed embolism, and 6 (0.44 per cent) died The disadvantage of such universal use of these drugs lies chiefly in their hemorrhagic tendencies We believe they are still useful after thrombosis and embolism have occurred Heparin is begun at once and takes effect promptly by prolonging the clotting time It is discontinued after the effects of dicumarol are noted The latter drug has its action on the liver where prothrombin is formed The normal prothrombin time by Quick's method is 17 to 19 minutes We usually give an initial dose of 300 milligrams of dicumarol the first day, and from 100 to 200 milligrams the 2nd day Thereafter, the daily requirement falls abruptly and only 50 milligrams may be needed to maintain the desired prothrombin time of 35 minutes It has been stated that a prothrombin time of 27 minutes or more will prevent thrombosis, and if it is kept below 60 minutes, hemorrhage will not occur Daily prothrombin estimates must be made to guide the therapy as a change may occur rapidly If hemorrhage occurs, prompt use of vitamin K and transfusion of whole blood is helpful in combating it until the prothrombin level falls Neither heparin or dicumarol will dissolve a thrombus already formed, but they will prevent propagation of the thrombus to a great extent Anticoagulant therapy is continued until all signs are again normal even to the measurement of the calf

Homan has stimulated much interest in femoral ligation There is no one measure which is as surely effective in arresting thrombosis Many operators advocate bilateral femoral ligation previous to major surgery in debilitated patients, as before prostatic resection and staged cancer surgery We have taken a middle course and utilized it only after thrombosis has been evidenced Many patients have been saved from fatality by femoral ligation even after one or more showers of pulmonary embolism have occurred Priestley found that if secondary emboli occurred, they developed within 10 days in 80 per cent of the patients When the patient does not make prompt progress after anticoagulant therapy, or if there is any sign of femoral thrombosis, we ligate Again, if there is any sign of propagation of the clot, we advocate immediate ligation Ligation is usually done only on the involved side, but we have seen instances where a secondary higher ligation or a contralateral ligation was eventually necessary The technic of ligation has been well stressed in Homan's work There should be no hesitancy to ligate the iliac or even inferior vena cava if the

femoral approach does not succeed in removing all proximal clot

The following case is one of many but it is reported to emphasize some of the salient points of the foregoing discussion

L V, a white male, age 22, was admitted to the hospital with a right indirect inguinal hernia which he had noted for 4 months. Only in the last 10 days had it been painful but he was able to keep it reduced at all times. He was in excellent condition and had never been ill enough to be hospitalized before. His height was 68 inches, weight 152 lbs, and muscular development fair to good. He was subjected to a hernia repair under spinal procaine (150 mg) anesthesia on December 23, 1943. It was noted that he did not move about in the bed too freely after operation and was cautioned about this. His oral temperature by December 27 was still 99.8 degrees F and the pulse 88. On search for the cause of this low-grade fever, tenderness was elicited in the calf of the left leg. On measurement this leg was 1 centimeter larger than its mate. Dorsiflexion of the foot produced pain in the calf, but the patient did not experience pain unless the leg was moved or the calf muscles gripped. He was not placed on heparin but 300 milligrams of dicumarol was given at once. The leg was elevated and a hot water bag placed on the calf. The initial prothrombin time was 18½ minutes. On the 2nd day, only two 50 milligram doses of dicumarol were given. The prothrombin time was then 25 minutes. Examination of the extremity revealed little change except that the measurement was now 2 centimeters greater than the other calf. By the morning of the 3rd day the patient suffered moderate pleural pain on the right with a mild hemoptysis and slight transient air hunger. This episode lasted but 10 to 15 minutes at most. Examination of the leg now showed tenderness in the left femoral region with little or no change in the calf. Prothrombin time was 38 minutes and the temperature level was elevated over the previous day, the highest reading being 102.4 and the lowest 100.0 degrees F. It was decided to do a femoral ligation at once. Under pontocaine (50 mg) spinal anesthesia, and in reversed Trendelenburg position, an 8 centimeter longitudinal incision was made over the left saphenofemoral region. The saphenous vein was ligated with fine silk and divided. The femoral sheath was incised inferior to the fossa ovalis and the femoral vein exposed. The vein was somewhat whiter and more thickened than normal. After placing two sutures around the vein loosely, a small opening was made in its wall and no blood flowed. One could see a thrombus lying within the lumen. With a glass-tipped aspirator, the clot was sucked out, bringing with it an elongated pointed free tail which had projected proximally 4 centimeters. Bleeding followed the removal of the thrombus and the ligatures were tied. The vein was then sectioned between additional suture ligatures at this level and the wound closed with interrupted fine silk in layers. Postoperatively dicumarol was continued at its previous level. Temperature receded gradually and was normal by the 3rd day after ligation. He did not have any further pulmonary symptoms nor did he show any hemorrhagic tendencies at the wound sites. Check-up roentgenogram of the chest revealed fairly normal findings. His leg was normal in measurement by the 8th day following ligation. There was no tendency to edema in the dependent position and he experienced no pain or tenderness. He was discharged on his 22nd postoperative day following the hernia repair. Dicumarol was stopped on the 9th day after ligation at which time he was ambulant.

## CONCLUSIONS

1) Postoperative pulmonary complications may be infectious, mechanical or circulatory. A review of the most important of these entities has been undertaken, viz atelectasis, spontaneous pneumothorax and pulmonary embolism.

2) Certain preventive measures will materially lessen the frequency of occurrence of most of the above complications.

3) The treatment of each complication is given briefly. Stress is laid on early recognition of each condition and prompt institution of therapy.

4) Several case reports are related to illustrate a few of the corollaries stressed in this treatise.

## CONCLUSIONES

1) Las complicaciones pulmonares postoperatorias pueden ser infecciosas, mecánicas o circulatorias. Se revisan las más importantes de ellas tales como la atelectasia, el neumotórax espontáneo y la embolia pulmonar.

2) Hay ciertas medidas preventivas que de hecho hacen menos frecuentes las complicaciones antes citadas.

3) El tratamiento de cada complicación se describe brevemente. Se recalca la importancia del descubrimiento temprano y el tratamiento pronto de las complicaciones.

4) Se relatan varios casos para ejemplificar los corolarios sobre cuya importancia se insiste en este trabajo.

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# Electrocardiographic Patterns in Pneumothorax\*

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This investigation was stimulated by our observation of certain changes in routine electrocardiograms taken on patients with pulmonary tuberculosis undergoing artificial pneumothorax therapy at this hospital. The study received increased impetus when a definite trend became evident. This consisted of significant EKG differences between the two groups, one receiving right and the other left pneumothorax. While the cardiograms of patients undergoing right-sided pneumothorax did not show a uniform and constant pattern of changes, those of patients receiving left-sided pneumothorax revealed a definite pattern. This difference was seen more predominantly in the chest leads. A review of the literature on this subject disclosed conflicting findings and opinions, which will be discussed subsequently.<sup>1 13</sup>

## *Method of Study*

This study includes 45 male cases, 43 with pulmonary tuberculosis undergoing artificial pneumothorax therapy, one case of spontaneous left-sided pneumothorax and one case of artificial pneumopericardium. Of the artificial pneumothorax group, 20 received right-sided pneumothorax only and with satisfactory collapse of varying degrees, 23 received left-sided pneumothorax only, 20 of which had satisfactory collapse and 3 were reported as unsuccessful. These cases were referred to us routinely from the Tuberculosis Section as soon as a decision for pneumothorax therapy was arrived at. Cases were selected only to the extent that patients with abnormal initial EKG tracings or patients who had already undergone pneumoperitoneum were excluded from the series.

The average age was 28.5 years ranging between 21 and 43. Sixty-two per cent of the cases were in their twenties and only four cases were over thirty-eight. None of the cases in the series had any evidence of heart disease. All but four of the cases reported had EKG tracings taken shortly before the initiation of

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\*From the Department of Medicine, Veterans Administration Hospital, Butler Pennsylvania

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collapse therapy These prepneumothorax cardiograms were all within normal limits All tracings were taken in the supine position with the three standard limb leads and CF-4 However, in selected cases CF-2 and CF-5 positions were added and in three of the left-sided cases the records were repeated in the standing, right lateral and prone positions, using the same leads After the initiation of pneumothorax serial tracings were started and continued The first postpneumothorax tracings were taken as early as the same day in some cases or as long after as one month In the great majority of cases, however, the first postpneumothorax tracings were taken within three to seven days Tracings were repeated at varying intervals and several patients (twelve cases) were followed for a period of six months or longer The longest period of follow-up in the right-sided group was nine months and in the left-sided group seven and a half months The case of spontaneous pneumothorax was followed for six months The case of artificial pneumopericardium was a 22 year old colored male who was being treated in the Tuberculosis Section under a diagnosis of tuberculous pericarditis with effusion This case is included in the series to compare the effect on electrocardiograms of air in the pleural cavity with that of air in the pericardial sac, as fluid was removed from the pericardial cavity and replaced by air X-ray films and EKG tracings were taken before and after the injection of air

### *Results*

#### *I The Right-Sided Pneumothorax Group*

The main electrocardiographic findings were as follows (See Figure II-E)

- a) Right axis shift—was seen in eight cases (40 per cent)  
This group includes six cases in which a definite S wave developed in L-1 and the QRS-1 which was mainly an upright deflection in the prepneumothorax tracing, became a diphasic or equiphasic complex, and two cases in which no S wave developed in L-1 and the QRS-1, which was mainly an upright deflection in the prepneumothorax tracing remained an upright deflection (R) but became much smaller in amplitude—no more than two or at most three millimeters in height
- b) Thus—there were altogether eight cases (40 per cent) with depression of QRS-1
- c) Depression of the P waves in one or more of the limb leads was seen in eleven cases (55 per cent) This was slightly more common in L-1 than in L-2 or L-3

d) T waves changes—The only T wave abnormality noted was depression or flattening of T-1 in ten cases (50 per cent) There was noted no T inversions or S-T deviations in the limb leads or the chest leads in any of the right-sided cases nor any right heart strain or P-pulmonale patterns X-ray plates and fluoroscopic observations of the chest done serially during the course of this study revealed no more than a minor degree of displacement of the heart to the left However, there was noted no definite correlation between the degree of displacement of the heart to the left and the degree of right axis shift

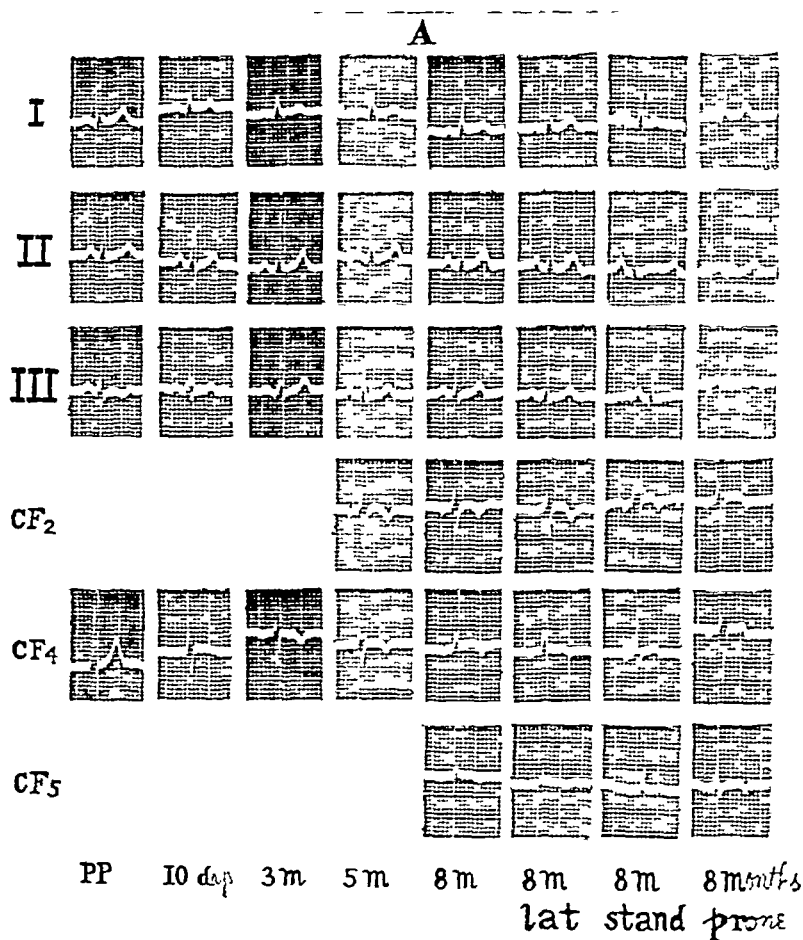


FIGURE I Case of left-sided pneumothorax age 26 Leads I II III CF-2 CF-4 and CF5 top to bottom Columns left to right—PP equals prepneumothorax tracing and tracings at varying intervals—10 days 3 months 5 months and 8 months Columns 5 to 8 all taken at 8 months after the initial pneumothorax in the supine right lateral standing and prone positions successively

## II The Left-Sided Pneumothorax Group

Of the twenty-three cases of artificial left-sided pneumothorax, twenty developed satisfactory collapse ECG findings in these twenty follows (See Figure I-A)

### a) Lowered Voltage of QRS-1

Lowered voltage of QRS-1 was noted in fourteen cases (70 per cent) This group includes those in which no S wave developed in Lead 1 but the QRS-1, which was an upright deflection in the prepneumothorax tracing, remained an upright deflection (R) but became much smaller in amplitude—no more than 2 or 3 mms in height

### b) Axis Shift

There were no cases in which a definite S wave developed in L-1 But, eight cases (40 per cent) showed slight degrees of right axis shift (small R-1, tall R-2 and tall R-3)

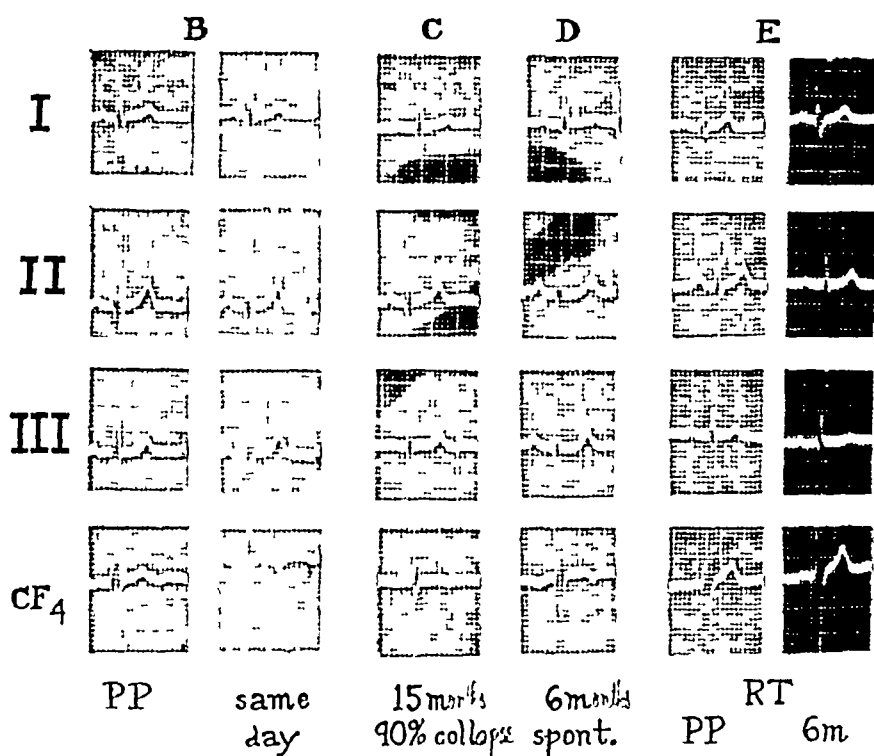


FIGURE II Leads I, II, III and CF-4 from top to bottom Columns left to right—Case "B"—left-sided pneumothorax, age 23, PP equals prepneumothorax tracing, and in next column, a tracing taken same day after the initiation of pneumothorax, with 40 per cent collapse Case "C"—age 21, left-sided pneumothorax, tracing taken at 15 months after initial collapse, with 90 per cent collapse Case "D"—age 33, left-sided spontaneous pneumothorax of 6 months duration with 75 per cent collapse Case "E"—right-sided pneumothorax, age 32, PP equals prepneumothorax tracing, and the next column, tracing taken 6 mos after the initial pneumothorax, with 60 per cent collapse

Left axis shift was not seen in any of the cases reported. Displacement of the heart to the right was noted in eleven of the cases but in only minor degrees. Again, no correlation was noted between the amount of displacement and the degree of axis shift.

c) Depression of P waves

Depression of P-1 was seen in only four cases (20 per cent)

d) T-changes in the Limb Leads

Thirteen cases (65 per cent) showed a lowered voltage or flattening of T-1 so that T-3s were thereby larger than T-1s

e) P-R and QRS Intervals

There were no cases of prolonged P-R or QRS interval and no definite pattern of S-T deviation in the limb leads

f) T changes in Chest Leads

All of the twenty cases (100 per cent) had T wave changes in one or more of the chest leads. These consisted of definite T wave inversions in all but one case. In the latter the T waves were merely flattened. The inverted Ts were peaked, symmetrical and with smooth shoulders bowed upward, thus resembling typical coronary T waves, and with S-T-T contour also of the coronary type (See Figure I-A, CF-4 in Column III-M)

g) Contour of QRS in Chest Leads

There was noted a definite change in the contour of QRS complexes in the chest leads. Nineteen of the twenty cases (95 per cent) had definite depression of R-4 to below 3 mm in amplitude. Twelve cases (60 per cent) developed prominent S waves in CF-4 which were absent or no more than 3 mm initially. In two cases the R waves were completely lost and QS waves became prominent. Six cases showed a lowering of voltage of both the R and S waves.

In twelve cases (60 per cent) multiple chest leads were taken, CF-2, CF-4, CF-5, once or twice during the course of the follow-up. In ten of the twelve cases the T waves in CF-2 and CF-5 were inverted together with those in CF-4, with the T wave inversions in CF-2 being more marked than in the other leads, while the QRS irregularities, especially that of lowered voltage, was more pronounced in CF-4 and CF-5 than in CF-2. Actually, the trend was towards more abnormal T waves in the right-sided leads and more abnormal QRS waves in the left-sided leads (Fig I-A)

The tracings in three cases of the left-sided pneumothorax group were repeated in various other positions than supine, such as, right lateral, standing, and prone, for comparison with tracings taken in the supine position. With this short series of three cases,

it is impossible to establish a trend, however, so much can be stated that regardless of the position used, T wave inversions were present in one or another of the three chest leads used (See Figure I-A, last 3 columns), although in the prone position the T wave inversions were the least marked and T waves were nearer to normal than in any other position. Littman,<sup>8</sup> and Feldman and Silverberg<sup>2</sup> state that the T wave inversions disappear in all other positions but the supine. Actually, in one of the three cases, the upright T waves in CF-2 taken in the supine position became moderately inverted in the prone position.

The three cases of left-sided pneumothorax classified as unsuccessful (no demonstrable collapse), showed no appreciable ECG changes.

The case of spontaneous pneumothorax (left) was followed for a period of six months. The initial T changes in the chest Leads were comparable to those found in patients undergoing left artificial pneumothorax. After six months follow-up the spontaneous pneumothorax persisted in spite of therapeutic attempts to obliterate the pleural cavity and thus re-expand the lung. The T wave inversions continued to be present although not to as marked a degree as was seen initially (Figure II-D).

In the one case of pneumopericardium, no appreciable difference was noted between the two electrocardiographic tracings taken just with fluid in the sac and then with air in the sac (See Figures III-B and A).

### Discussion

Abnormal ECG patterns have been noted in patients receiving pneumothorax therapy and have been discussed many times in the literature.<sup>1-13</sup> However, the striking differences in ECG pat-

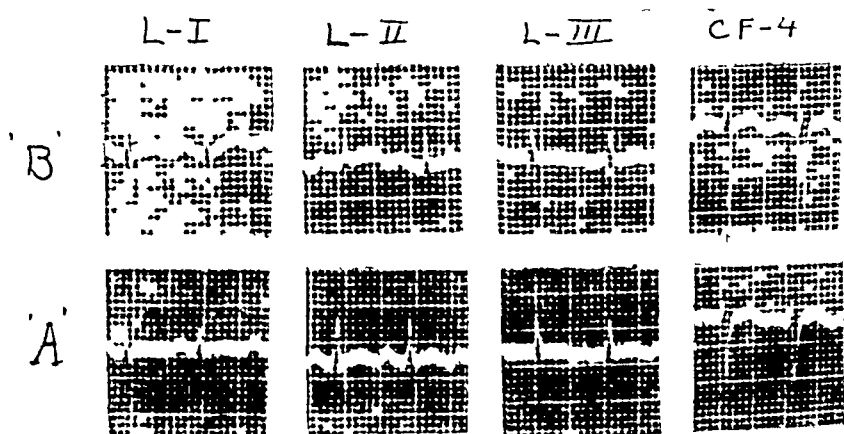


FIGURE III ECG—Leads I, II, III and CF-4—from left to right "B"—tracing taken with fluid in pericardial sac "A"—tracing taken with air in pericardial sac

terns between right and left pneumothorax were not clearly demonstrated until comparatively recently. Then Miller,<sup>11</sup> in 1945, reported a series of cases all with left pneumothorax and "mediastinal emphysema," demonstrating a pattern with low T waves in Lead-1, and flat or inverted T waves, elevated S-T segments and small or absent R waves in the 4th Lead. Littman,<sup>8</sup> in a short series, more or less supported Miller's previous observations but pointed out that these abnormal findings were present only in the supine position. He concluded that the ECG alterations were the result of the presence of air between the heart and the exploring electrode. Previous to this it had been suggested that the ECG changes were due to an alteration in the coronary circulation.<sup>12</sup> Still other investigators, notably Goldberger and Schwartz,<sup>4</sup> believed that the rotation of the heart about one or more of its three axes could account for the ECG alterations which they noted in cases of pulmonary tuberculosis with collapse. More recently Feldman and Silverberg,<sup>2</sup> concluded that these ECG changes in left-sided pneumothorax were due to a combination of displacement of the heart and interposition of air between the heart and the chest wall.



FIGURE IV Case of tuberculous pericarditis  
age 22 X-ray film of chest in P-A

In our series we have shown a definite pattern of ECG changes in the left-sided pneumothorax group. The most conspicuous of these changes are the T inversions in the chest leads which occurred in all but one of our reported cases. In the right-sided



cases, these T inversions are notably absent, and the only abnormal pattern has been a tendency to right axis shift and depression of the P waves in the limb leads. In the left-sided group, the T wave inversions, as well as the other changes, have appeared as early as the same day of collapse in many cases (Figure II-B), while in others, there has been a gradual depression of the T waves with eventual inversion in a course of days or weeks (Figure I). In the majority of cases the QRS depression both in Lead I and in CF-4 has appeared earlier than the T inversion. With the exception of three cases, all T wave changes have persisted to the end of this study. In these three cases the T inversions reverted to normal and remained normal in spite of the presence of air in the pleural cavity and maintenance of satisfactory collapse. We are unable to state at this time how long these changes



FIGURE V Same case as in figure 4, in a right-sided lateral decubitus position, taken after fluid was aspirated and air injected into the pericardial sac

will tend to persist. However, one case that was observed fifteen months after the initiation of pneumothorax still maintained the characteristic changes in CF-4 (Figure II-C). Thus, it might be assumed that these changes may persist as long as the pneumothorax is maintained. Our findings differ from those of Littman,<sup>8</sup> and others,<sup>2</sup> concerning the disappearance of the T inversions in other positions than supine. We have shown such T inversions in one or more chest leads in other positions than supine, i.e., in right lateral, standing and prone (Figure I). The T inversions are most conspicuous in the supine position and least so in the prone

It is interesting to note that the shift of electrical axis when

it occurs is always to the right, regardless of the side of the chest undergoing pneumothorax. We have found this axis shift to the right to be more common in right than in left pneumothorax. This finding is comparable with that of Treiger and Lundy<sup>13</sup>. We have seen no definite correlation between the amount of heart displacement and the degree of axis shift, and no correlation whatsoever between the percentage of collapse and the degree of T inversion or any of the other changes described. This is very well demonstrated in Figure II, in cases B and C where the T inversion in case C with 90 per cent collapse is much less striking than in B with only forty per cent collapse. In the one case of spontaneous left-sided pneumothorax the changes are comparable with those in artificial left-sided pneumothorax (Figure II-D). However, Master,<sup>10</sup> expresses the opinion that the changes in spontaneous pneumothorax are usually more marked than those in artificial cases.

As for the causes effecting these changes, it seems likely that a combination of factors are at work. The fact that these abnormal T waves resemble coronary T waves have suggested to some authors the possibility of changes in the coronary circulation.<sup>8,12</sup> The lack of clinical evidence of coronary disease or insufficiency as well as the lack of other coronary ECG patterns make this hypothesis unlikely. We believe that displacement of the heart *alone* is also an unlikely factor, as regardless of the direction of the displacement of the heart the electrical axis shift always happens to be to the right. Also, in spite of the presence of displacement and axis shift, we were unable to show T inversions in the right-sided cases. A more plausible factor, we believe, is the presence of air in the pleural cavity situated between the heart and the chest wall and acting as a poor conductor.<sup>7,8</sup> Considerable evidence is present to support this hypothesis although not conclusive: the fact that the T inversions are found only in the left-sided cases, and the fact that these T inversions are absent or much less striking in cases of left-sided collapse effected by left-sided thoracoplasty. However, there are several undeniable arguments against the air hypothesis: (1) There is no correlation between the percentage of collapse and the degree of T inversion. (2) T changes persist in other positions than supine, such as in right lateral, standing and prone, although not to as striking a degree as in supine. (3) In three cases in our series the inverted T wave reverted to normal in spite of the maintenance of collapse and continued presence of air in the pleural cavity. (4) In the one case of pneumopericardium reported the ECG pattern was similar before and after the introduction of air into the pericardial sac (Figure III). It would be reasonable to assume that an amount

of air (100 cc) in a smaller cavity, namely the pericardial sac, would be more effective or at least as effective in bringing about such ECG changes as are observed when air is present in the pleural cavity, a much larger space. We believe that probably rotation of the heart rather than displacement is another factor to be considered, and that both rotation and air as well as other unknown factors working in combination might be responsible for these changes.

### SUMMARY

1) Forty-five cases have been presented, forty-four with pneumothorax of one or the other side, and one with artificial pneumopericardium, with serial electrocardiographic studies before and after the initiation of pneumothorax or pneumopericardium.

2) Characteristic ECG patterns both in right and left sided pneumothorax have been shown and described.

3) A marked and definite difference in these ECG patterns between the right and left sided groups has been shown and illustrated.

4) The ECG pattern in the right sided group has been mainly a tendency to right axis shift, depression of QRS-1, and depression of P waves in the limb leads. T inversion has been notably absent.

5) The ECG pattern in the left sided group has been more conspicuous and more striking, and has consisted of a lower voltage of QRS-1, flattening of T waves in Lead I, a change in the contour of QRS complexes in the chest leads, and a definite inversion of T waves in the chest leads, these T wave inversions being the most constant and conspicuous of all changes.

6) The T wave inversions have persisted in various other positions than supine, namely, standing, right lateral and prone.

7) As for the basic cause effecting these changes, the evidence is not conclusive. However, available evidence points to rotation of the heart and the presence of air between the heart and the chest wall as very probable causative factors.

*Note.* We wish to express our thanks and gratitude to Doctors George C. Glinsky, A. C. Cohen, and L. H. Hetherington for their generous help and suggestions during the course of this study.

### RESUMEN

1) Se han presentado cuarenta y cinco casos, cuarenta y cuatro con neumotórax de uno o el otro lado y uno con neumopericardio artificial, con estudios electrocardiográficos seriados antes y después de iniciar el neumotórax o el neumopericardio.

2) Se han demostrado y descrito patrones electrocardiográficos

característicos, tanto del n  
izquierdo

3) Se han demostrado e  
diferencias en estos patrones  
del lado derecho y del izquierdo<sup>4</sup>

4) El patron ECG en el grupo  
palmente una tendencia a des  
de QRS-1 y depresión de las on  
extremidades Ha sido notable la a

5) El patrón ECG en el grupo del  
conspicuo y más notable, y ha consisti  
QRS-1, aplastamiento de las ondas T en  
en el contorno de los complejos QRS en  
y una inversión bien definida de las ond  
del torax, la inversion de estas ondas T ha  
y conspicuo de todos los cambios

6) Las inversiones de las ondas T han persis  
ciones además de la boca arriba, a saber, de pies,  
y boca abajo

7) No se ha determinado conclusivamente la causa  
que influencia estos cambios Sin embargo, las prueb  
indican que la rotación del corazon y la presencia de  
corazón y la pared toracica probablemente son los factores

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# Abstract of Replies to a Questionnaire on Intrapleural Artificial Pneumothorax\*

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To obtain the present opinions on pneumothorax, a questionnaire was sent to a number of physicians who have been working in this field for a long time and have, with few exceptions, been engaged in teaching. Questions bearing on pneumothorax, other than the length of time it should be continued under different conditions, were asked.

These questions were (1) In what percentage of patients is pneumothorax now employed? (2) How long is successful pneumothorax continued, (a) in cases with cavitation, (b) in others? (3) Is pneumothorax used as an adjunct to the rest regimen? (4) If so, are patients given a three to six months period of rest, to determine if their disease will come under control, before the institution of pneumothorax? (5) When pneumothorax is instituted, are patients kept at rest for a prolonged period—a minimum of six months? (6) Are patients treated with ambulatory pneumothorax, that is, without having more than a few weeks of bed rest following the induction of the pneumothorax?

There were 90 replies. Many physicians manifested considerable interest by writing at some length. A few gave indefinite answers which could not be classified. Some stated that they wished to know the optimal time to discontinue a successful pneumothorax. These men asked to be informed of any conclusion drawn from this survey.

There was no unanimity of opinion in the replies to any of the questions. The proportion of the patients, under the care of the interrogated group of physicians, on whom pneumothorax is established or on whom an attempt is made to establish pneumothorax varies from 4 per cent to 100 per cent.

A Saranac Lake physician whom, incidentally, I saw give the first pneumothorax I had ever witnessed 30 years ago this summer, said he believed that in the last 10 years we have come to the realization that pneumothorax, in the long range view, is a dangerous procedure and that the whole subject needs periodic going over and re-evaluation.

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\*Round Table Discussion, 14th Annual Meeting of the American College of Chest Physicians, Chicago, Illinois, June 20, 1948

Eight of the physicians said they are using pneumothorax in 10 per cent of their patients. This was the greatest number of men employing pneumothorax in the same percentage of patients. One physician who has been treating tuberculous patients for more than 30 years replied that he now uses pneumothorax in only 10 per cent of his cases where ten years ago he employed it in 35 per cent. He said that all of his colleagues at Saranac Lake as well as most physicians in the East are using pneumothorax less frequently than in former years. They are trying to avoid tuberculous empyema which 15 to 25 years ago occurred in 16 to 18 per cent of their pneumothorax cases. They believe a high proportion of empyema is avoided by using pneumothorax in early cases and not in those with more advanced disease with peripheral involvement. One physician reported only one case of empyema complicating pneumothorax in the past four and one-half years. He thought this was due to better management of patients. The one occurred in an un-cooperative patient.

The reason given in general for the present less frequent use of pneumothorax is to avoid complications. Apparently more physicians are offering patients an opportunity to overcome their disease on the rest regimen without instituting pneumothorax or at least before it is established. This course is followed with an appreciation of the meaning of rest as it applies to a patient with tuberculosis as well as an understanding of its limitations. It also appears that instead of the more indiscriminate use of pneumothorax there is a more frequent use of paralysis of the diaphragm, pneumoperitoneum, primary thoracoplasty and primary resection and, more recently, the use of streptomycin in carefully selected cases. Primary thoracoplasty apparently is being used more frequently in patients especially past middle life and particularly where the disease is limited, for the most part to a cavity in the apex. There also appears to be a fairly general feeling that where the upper lobe is largely destroyed by the disease and where there is involvement of the larger bronchi, other conditions permitting, primary thoracoplasty and at times primary resection offer the best possibility for the permanent control of the tuberculous.

One physician regarded pneumothorax to be a valuable type of treatment if properly handled but he felt that it is frequently abused and mishandled and blamed for much of the operators' shortcomings and lack of experience. Another believed that each patient is a case unto itself and should be cared for as an individual, not by mass therapy. One with more than 30 years of experience, stated that he employs pneumothorax regardless of the stage of the disease in every patient on whom it could be

established. He apparently tries pneumothorax on all patients. Other opinions varied between these extremes. The opinion was expressed that indications for the use of pneumothorax and for its termination, as well as for all the other phases of treatment, must be based on a clear concept of the pathogenesis of tuberculosis as well as on the knowledge of the pathological physiology in any particular case. In emphasizing the importance of rest in treatment, this physician said pneumothorax does not influence the basic reaction between the invading organism and the cellular reaction of the host.

A physician working in one of the oldest institutions in the New England area wrote that he starts pneumothorax at once in the following cases: (a) Those with a cavity over 2 centimeters in diameter; (b) Those with large cavities which are not of the tension type; (c) Those with smaller cavities with recent spread of disease in the same lung; (d) Those with involvement which exceeds more than a third of the lung and is of the honeycomb or the ulcero-exudative type; (e) Those with unilateral disease who have hemoptysis of more than two tablespoons of bright red blood not controlled otherwise; (f) In the above cases the patients must be between 12 and 50 years of age, the function of the heart good, the vital capacity not less than half its normal amount (judging by estimation of the diaphragmatic movement by fluoroscopic examination) and absence of emphysema and an acute stage of asthma. This physician stated that ambulatory pneumothorax is used in many patients.

The time element in pneumothorax is reckoned from closure of cavities and/or sputum conversion.

In discussing the duration of pneumothorax, one physician commented: "Individualization is the basic factor, generally speaking, in determining how long pneumothorax should be continued." A number of physicians said the termination depended upon many factors, such as the size, complexity and location of the cavitation, the thickness or thinness of the cavity walls, the amount of additional parenchymal disease, the effectiveness of the pneumothorax, presence or absence of complications and associated bronchial disease, etc. One physician stated that under certain conditions pneumothorax should be continued for life, but he did not specify the conditions.

A physician who was among the first to use pneumothorax in tuberculosis in this country, said that after three years, in cavity cases, he allows the lung to expand slowly. If there are signs that the cavity is not closed or there is recurrence or increase of cough and expectoration, the pneumothorax is continued for another year or more. Then another attempt is made to let the lung expand.

Another physician replied that more recently he has been terminating pneumothorax after shorter intervals than formerly in order to avoid pleural complications that are always a threat as long as pneumothorax is present. However, he felt that in the past, expansion was often allowed to take place too soon because of the absence of planigrams and gastric lavage which now make more accurate observations possible. This same physician believes that if pneumothorax does not accomplish its purpose in two or three years, thoracoplasty is needed to prevent relapse.

Most of those commenting on the time element of pneumothorax directed their remarks to the handling of cavity cases. There were four or five physicians who stated that they did not use pneumothorax in the absence of cavitation. One said that unsuccessful pneumothoraces are many times carried on too long, and that the indiscriminate continuation of successful pneumothorax on a time basis without knowledge of or regard for the original condition as an indication should be condemned. One physician said that there is nothing so important as the judgment to determine when pneumothorax should be terminated.

The majority of physicians stated that they use pneumothorax only as a supplement to the rest regimen. The larger proportion stated that unless there are specific indications why pneumothorax should be established without a prolonged delay, they prefer to have their patients experience a period of three to six months rest. This, in general, meant what is ordinarily termed "typhoid rest." These men were of the opinion that a fairly large proportion of patients that have an opportunity to carry out rest in its true sense, especially during the early or acute stage of their disease, will overcome their disease in a reasonable length of time without the use of mechanical therapy.

The majority of physicians were not in favor of ambulatory pneumothorax, that is, instituting the treatment under conditions where the patient is either not put to bed at all or for only a few weeks. Many physicians who oppose this type of treatment expressed their feelings by such answers as "absolutely not," "definitely no," and one man in a position to observe end results from many sources asked the question, "Is that treatment?" One man stated, "Mere collapse of the lung does not mean that the lung is healed—healing will occur more rapidly and more surely if the collapse is carried out in connection with the rest regimen and there will be fewer complications." Another stated that he, "looks upon tuberculosis as a generalized disease and believes that in its treatment rest for the body as a whole is the important factor." One physician commented in referring to ambulatory pneumothorax, "You are asking for trouble if it is done very often."



The majority of physicians who use ambulatory pneumothorax stated that they carry out this type of treatment only under unusual circumstances, such as where facilities for bed rest are not available. One replied, "I have many cases under ambulatory pneumothorax treatment. Most of my cases are started in general hospitals and it is almost a practical necessity to use ambulatory pneumothorax treatment because I am not able to keep the patient in the general hospital any length of time." Another said that he used ambulatory pneumothorax quite extensively and stated, "I am beginning to believe this is a justifiable form of treatment." Another physician who stated that he institutes pneumothorax in his office and if necessary sends patients home in an ambulance, said that he was of the opinion that criticism of ambulatory pneumothorax is definitely unwarranted.

It appears from the answers to these questions that there is a tendency to use pneumothorax less frequently in the treatment of pulmonary tuberculosis, primarily because of the hazards pneumothorax involves. There appears also to be some increase in the use of other forms of mechanical therapy which, at times at least, supplant pneumothorax. It seems evident, too, that, in general, rest in its more comprehensive meaning is being recognized more and more as the basic factor in the treatment of pulmonary tuberculosis. Twenty-five years ago, Allen Krause wrote that rest alone had returned thousands of individuals to health and a productive life. More recently, Max Pinner wrote that "the very foundation of all treatment of active pulmonary tuberculosis is rest" and continuing he said, "How highly the therapist estimates the therapeutic efficiency of rest depends largely upon his willingness to give it a complete and thorough trial over a sufficiently long period of time and on his clear recognition of the limitations of a pure rest regimen." He then pointed out that just being in bed does not constitute bed rest for the tuberculous patient. True rest for the tuberculous is secured only by the physician's psychological control of the patient—a control made possible only by the physician taking the patient into his confidence and explaining to him his disease as well as the cure with all its intricacies and by providing an environment that is conducive to his adjustment to the cure.

Finally, in evaluating the effectiveness of any phase of the treatment of pulmonary tuberculosis it is essential to bear in mind that at a certain proportion of patients, estimated to be about one out of every four, will overcome their disease without treatment or regardless of treatment. They are the patients with the resolving type of pulmonary tuberculosis. Unfortunately, at the outset it is not possible to determine which patients will and which

patients will not need treatment. They must all be treated with judgment and caution until the course of their disease is definitely evident. When the possibility of the spontaneous recovery from tuberculosis is not taken into consideration, conclusions as to the value of certain factors in treatment may be misleading.

Number of Cases	Percentage of Patients Given	Number of Cases	Number Years Pneumothorax Given in Cavity Cases	Number of Cases	Number Years Pneumothorax Given in Cavity Cases
1	4	1	1 $\frac{1}{2}$ -3 yrs	1	1 $\frac{1}{2}$ -1 yr
4	5	4	2 yrs	1	1 $\frac{1}{2}$ -3 yrs
8	10	4	2-3 yrs	1	1 yr
3	15	1	2-4 yrs	3	1-1 $\frac{1}{2}$ yrs
1	15-25	4	2-5 yrs	8	1-2 yrs
6	20	2	2 $\frac{1}{2}$ -3 yrs	4	1-3 yrs
2	20-25	8	3 yrs	15	2 yrs
2	25	10	3-4 yrs	8	2-3 yrs
7	30	12	2-5 yrs	6	2-4 yrs
2	30-35	1	3-6 yrs	11	3 yrs
1	30-40	3	3 $\frac{1}{2}$ -5 yrs	5	3-4 yrs
6	35	5	4 yrs	1	3-5 yrs
2	40	6	4-5 yrs	1	5 yrs
7	50	11	5 yrs		
6	60	1	5-8 yrs		
1	65	1	7-4 yrs		
2	70	1	Indefinitely		
2	75				
1	85				
1	90				
2	95				
1	100				
Answers to Question No III				Yes 62	No 17
Answers to Question No IV				Yes 48	No 29
Answers to Question No V				Yes 59	No 21
Answers to Question No VI				Yes 11	No 50
Ambulatory Pneumothorax Given Only Under Unusual Circumstances					18

13 physicians out of 70 use pneumothorax in 10 per cent or less of their patients

29 physicians out of 70 use pneumothorax in 25 per cent or less of their patients

45 physicians out of 70 use pneumothorax in 35 per cent or less of their patients

54 physicians out of 70 use pneumothorax in 50 per cent or less of their patients

24 physicians out of 78 continue successful pneumothorax for 3 years or less in cavity cases

33 physicians out of 68 continue successful pneumothorax for 2 years or less in cases without apparent cavitation

# Treatment of Aortic Aneurysms by Wrapping with Foreign Body\*

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The distorted anatomy, invasive tendencies, large size, and friable thin walls of both syphilitic and arteriosclerotic aortic aneurysms contraindicate any attempt at extensive surgical manipulation in the form of resections and anastomoses of these aneurysms. The pounding, pulsating pressure exerted by these aortic dilatations presents an almost malignant tendency to invade and penetrate any adjacent soft tissue. Even the walls of the bony thorax can be eroded by an expanding pulsating aneurysm.

The intense foreign body reaction produced by cellophane and impure polythene film with its constricting fibrosis seems to offer the simplest and most satisfactory method of at least curbing the expansion of these aneurysmal dilatations. This possibility was suggested by the report of Harrison and Chandy<sup>1</sup> who had gradually eliminated two arteriovenous aneurysms of the subclavian vessels by cellophane. Harrison's clinical application of the material resulted from the report of Pearse,<sup>2</sup> who had demonstrated the ability of cellophane to produce gradual obliteration of the lumen of important blood vessels, such as the internal carotid, in the place of the previously devised and somewhat unsatisfactory clamps and bands. This constricting property of cellophane had been demonstrated originally by Page,<sup>3</sup> who used it in 1939 to produce artificial nephritis and hypertension in dogs by wrapping it around the kidneys.

A dilemma arose, however, from the reports of McKeever<sup>4</sup> and others that cellophane produced no reaction and was suitable for reconstructing tendon sheaths and lining joint spaces. An experimental study was undertaken at Washington University School of Medicine with several chemically different varieties of cellophane and plastic material, supplied through the courtesy of the DuPont de Nemours Company of Wilmington, Delaware. The results of this investigation published in greater detail elsewhere,<sup>5</sup> suggested that a new impure plastic known as Polythene film produced the most intense foreign body reaction, whereas some of the other types produced little if any reaction. This fibrotic

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reaction produced by the impure polythene film was somewhat surprising since it was supposed to have been chemically inert. Considerable confusion has arisen during the past year since Ingraham, Alexander and Matson<sup>6</sup> reported pure polythene especially refined for medical use to be physiologically inert and suitable for covering exposed brain tissue. This was not the result observed by Renault and myself in our animal experiments with impure polythene film supplied by the DuPont Company (Figs 1, 2 and 3). Hasty comparison of results with other experimental research workers in various parts of the country indicated that four other groups had obtained definite scar tissue formation from the use of impure polythene film obtained from the DuPont Company. Several others are still carrying on animal experiments but do not have their final results available as yet. Yaeger and Cowley<sup>7</sup> recently reported their experimental results at the American Surgical Association Convention in Quebec in which the contaminant dicetyl phosphate present in the DuPont polythene film was found to be the irritating factor. It is hoped that polythene film with an even greater percentage of dicetyl phosphate can be obtained for further experimental work to create a more intense reaction and fibrosis.

Impure polythene film was selected, therefore, to wrap aneurysms of the thoracic aorta to induce an intense foreign body fibrous tissue reaction around the aneurysm, thereby preventing its further expansion and rupture.

### *Operative Technique*

The patient is placed on the side opposite the aneurysmal dilatation of the thoracic aorta using endotracheal ether and oxygen. Through a para vertebral incision extending around the angle of the scapula, the entire length of the fifth or sixth rib is resected and the pleura opened through the bed of the resected rib. The lung is retracted and the mediastinal pleura dissected free from the aneurysm, exposing as much of the surface of the diseased aorta as can be safely freed without danger of rupture. It is frequently impossible to free the entire circumference of the descending aorta because of beginning erosion of the vertebrae and ribs around the origins of the intercostal vessels. The pleura may be too attenuated and adherent over the thin bulging areas to permit its complete removal. A sheet of impure polythene film is then cut to fit the dilated portion of aorta without extending over adjacent normal structures. This film is then sutured loosely to any suitable mediastinal tissue with fine silk sutures, care being taken not to pass any sutures directly into the wall of the aneurysm.

One other saccular aneurysm of the ascending aorta was ex-

## SUMMARY OF RESULTS

Polythene film was used to wrap or patch the nine syphilitic aneurysms of the thoracic aorta reported below

No	Name	Place	Place	Type	Location	Symptoms	Result
1	W W	7/ 6/45	Barnes Hosp , St Louis, Mo	Fusiform	Descending aorta	Pain anterior and posterior chest	Complete relief of pain 1 yr later
2	L P	10/11/45	Colored City Hosp , St Louis, Mo	Saccular	Ascending aorta	Pain anterior chest and weakness	Cannot be traced, believed dead
3	J E	12/ 8/45	Barnes Hosp , St Louis, Mo	Saccular and fusiform	Ascending aorta and innominate	Chest pain and weakness	Relief of pain but tires easily
4	D H	1/ 2/46	White City Hosp , St Louis, Mo	Saccular	Ascending aorta	Cough and pain anterior chest	Cannot be traced, believed dead
5	F K	11/29/46	Good Samaritan Hosp , Portland, Oregon	Fusiform	Descending aorta	Cough and chest pain	Relief of chest pain, died, hemorrhage esophagus 1 1/2 yrs later
6	W H	1/16/47	Veterans Hosp , Portland, Oregon	Fusiform	Distal arch and descending aorta	Chest pain	Relief of pain
7	J L	6/28/47	County Hosp , Portland, Oregon	Fusiform	Distal arch and descending aorta	Chest pain, chronic cough, Hemoptyses and dyspnoea	Died, hemoptysis
8	C E	7/10/47	Veterans' Hosp , Portland, Oregon	Saccular and fusiform	Ascending aorta	Anginoid pain on exertion	Moderate relief of pain, increased exercise tolerance
9	A J	9/22/47	St Vincents Hosp , Portland, Oregon	Saccular and fusiform	Distal arch	Posterior chest pain and dysphagia	Died, hemorrhage 3 months later

plored at the Portland Veterans' Hospital but found unsuitable for wrapping due to erosion of the anterior chest wall and inability to dissect away the superior vena cava which was imbedded in the aneurysm wall. Several other patients have been considered unsuitable for surgery either because of severe cardiac decompensation or obstruction of the left main bronchus by pressure from the aneurysms.

Four of the nine patients whose aneurysms were reinforced by polythene have already survived from one to three years with moderate to complete relief of symptoms of pain in all cases. A period of from three to six months was required to obtain maximum benefit in most patients. Little if any improvement has been noted in strength, although the relief of pain has permitted one patient to return to full time employment and the other three to increase their activities. The patient who died of rupture of his aneurysm into the esophagus one and one half years after wrapping had obtained considerable relief of his pain and resumed light work six months after his operation.

### *Comments*

Relief of the throbbing, pulsating anterior chest pain or the constant dull ache in the back appears to be the most gratifying result of wrapping these intrathoracic aortic aneurysms. Although the original purpose of the procedure was to patch or reinforce weakened artery walls and prevent or delay their rupture, the patients frequently seem more concerned about their immediate symptoms. The one patient who has been examined at autopsy one and one half years after wrapping his aneurysm failed to show any actual shrinking of the aneurysm cavity, although the vessel wall was thickened by a layer of fibrous tissue on both sides of the polythene film. The lack of any decrease in size of the x-ray shadows is to be expected from the pathologic reaction noted in animals in which a thick layer of dense scar tissue is deposited on both sides of the film.

Fusiform aneurysms of the descending aorta offer more favorable opportunities for successful reinforcing with impure polythene than the saccular aneurysms of the ascending aorta and its arch for the following reasons. They are more accessible with less important branches and adjacent vital structures offering a wider surface for covering. They are more apt to produce pain which can be relieved by wrapping. The incidence of cardiac involvement with aortic insufficiency and decompensation appears to be lower in this group.

An obstruction of one of the main bronchi or encroachment on the trachea presents an absolute contraindication to surgery.

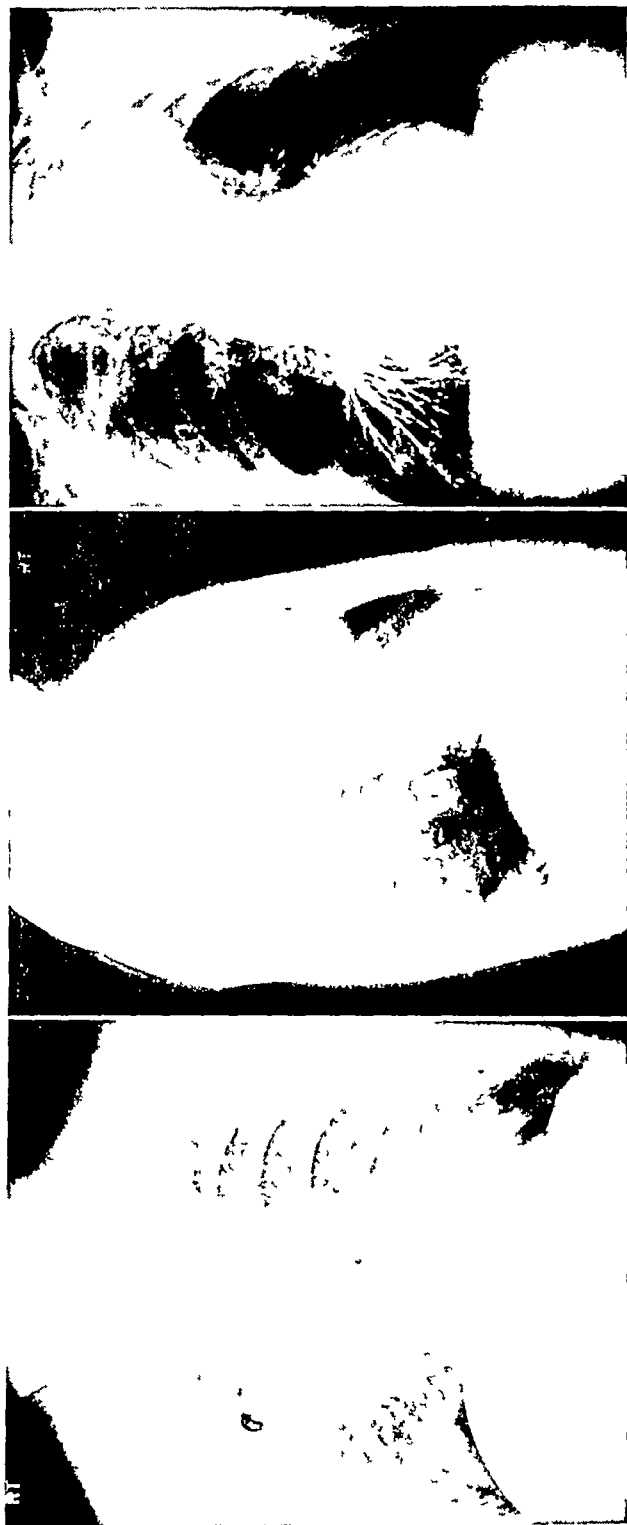


FIGURE 1

FIGURE 2

FIGURE 3

*Figure 1 and 2 together* Preoperative chest x-rays of J E No 3, with sacular syphilitic aneurysm of ascending aorta, which was wrapped with polythene film two and one half years ago. This patient is still alive without chest pain although the aneurysm was about to involve the anterior chest wall at the time of operation—*Figure 3* Preoperative bronchogram on J L No 7, with sacular syphilitic aneurysm of distal arch of aorta. Bronchogram failed to show obstruction of left main bronchus indicating suitability for surgery

Severe cardiac decompensation with insufficiency of the aortic valve or erosion of the anterior chest wall both preclude any very satisfactory end result from the procedure even though the patient may withstand the immediate surgery. Arteriosclerotic aneurysms of the abdominal aorta also can be reinforced satisfactorily with impure polythene provided the disease has not already interfered with the circulation of the lower extremities.

### CONCLUSIONS

1) Commercial unrefined polythene film has been shown experimentally to produce an extensive fibrous tissue proliferation when placed within the body.

2) This irritative reaction is apparently due to chemical substances added to the pure polythene during its processing.

3) This fibrous tissue reaction of polythene can be employed to reinforce the weakened vessel walls of aneurysms.

4) Nine patients whose intrathoracic aneurysms have been wrapped or patched with polythene are reported.

5) Five of the patients survived for one to three years after surgery with varying degrees of improvement in their symptoms.

6) Four of the patients are still alive, the others having succumbed to their disease.

### CONCLUSIONES

1) Se ha demostrado experimentalmente que películas de polietileno comercial no refinada producen una proliferación extensa del tejido fibroso cuando se las coloca dentro del cuerpo.

2) Aparentemente se debe esta reacción irritante a sustancias químicas que se añaden a la polietileno pura durante su preparación.

3) Se puede utilizar esta reacción fibrosa de la polietileno sobre los tejidos para fortalecer las paredes debilitadas de aneurismas de vasos sanguíneos.

4) Se informa sobre nueve pacientes cuyos aneurismas intratorácicos han sido envueltos en polietileno o remendados con esta sustancia.

5) Cinco de los pacientes sobrevivieron de uno a tres años después de la operación con varios grados de mejoría de sus síntomas.

6) Cuatro de los pacientes viven todavía, mientras que los otros han muerto de su enfermedad.

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## D I S C U S S I O N

OSLER ABBOTT, M D , F C C P  
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It is a great pleasure to discuss Dr Poppe's paper because I have many pleasant memories of working with him and it was his work that instigated my interest in the subject I would like to emphasize that I think both our interests were fundamentally aroused in this subject by Dr Evarts Graham This work is still in an experimental phase It has been our policy to consider that experimental surgery must be done essentially on hopeless cases The individuals on whom we have done this work in Atlanta have, in the main, been patients who came in with the diagnosis of cardiac decompensation or pneumonia in one or both sides These are the patients Dr Poppe mentioned as being non-candidates for the operation They have been our main candidates and we have learned many things from them

I would particularly like to emphasize the statement of over-soaking in alcohol as we had a sad experience of no reaction at all from the material used after it was soaked too long a time The boiling method is much better A few slides will show how we have attacked this problem much of which is purely experimental surgery on the hopeless case In many cases we have been pleased, in others we have been most displeased, and we feel there is much more to learn about the problem Certainly in our experience of following up patients who have had partial wrapping of the aneurysms, the results have been quite poor, only 40 per cent of them have had relief of pain and the majority of them that we have had a chance to follow have ruptured the aneurysm within one or two years after the operative procedure We now make it a routine method, that whenever we wrap an aneurysm incompletely there is concomitant internal wiring of the aneurysm We have now operated on 32 patients, in whom the aneurysm has been wrapped, and there have been six more in whom decompression has been done, many of whom have felt so well that they have refused further surgery and have thus given us

a comparative series as to what life expectancy is in the decompressed and in the wrapped. Certainly, with decompression there is prolongation of life, but unfortunately the decompression does not last a sufficient length of time to give us a permanent aid, they usually come back with return of symptoms of bronchial compression within about four months after recompression

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JAMES E DAILEY, M D, F C C P  
Houston, Texas

We have had the opportunity to wrap three of these aneurysms in the past year, one of the ascending aorta, one of the descending aorta and one of the innominate. The results of course are difficult to evaluate, other than the fact that the patients are relieved of their symptoms of pain and disability and, in our three cases, the patients were completely relieved and are back at work. There was absence of progression of the tumors as seen on the x-ray films. In the case of the aneurysm of the innominate, which could be seen and felt, there was distinct regression in the size of the tumor and absence of visual and tactile pulsations.

With regard to sterilization of the cellophane and the effect that soaking in alcohol has on the substance, we sterilize it by immersion in cyanide solution with apparently good results

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### *Closing Remarks*

*J Karl Poppe, M D, F C C P* I should like to congratulate Dr Abbott on his large series of cases and on his courage in tackling some of these poor risk patients. We know that the more advanced the lesion, the less satisfactory the result. The most favorable results to date in my experience have been with aneurysms of the descending aorta, in which there is less apt to be cardiac complications such as aortic insufficiency and cardiac decompensation. In patients with only pain from involvement of the chest wall and intercostal nerves the possibility of relieving symptoms seems much greater.

A recent communication received from the Dupont Company states that the diacetyl phosphate is slightly soluble in cold alcohol and much more soluble in warm alcohol, suggesting that one might possibly sterilize polythene film in alcohol if kept in the refrigerator, but boiling seems still better.

# Nutrition in Far Advanced Tuberculosis

## A Preliminary Study\*

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This study was initiated to attack the problem of establishing nutritional balance in far advanced pulmonary tuberculous patients and to observe, if possible, whether a proper nutritional balance, in itself, could favorably deflect the downward course of these patients. It was evident that the invariably poor appetites of these patients should be the first point of investigation.

The study of appetite has developed considerable experimental work. There is evidence that the sensation of hunger is directly correlated with increased gastric tone and secretions, this was evident in the fasting experiments of Hoelzel<sup>1</sup> and the x-ray observation of Barclay.<sup>2</sup> Glaessner,<sup>3</sup> in 1943, offered experimental evidence that gastric tone and secretory activity varied inversely with blood sugar volumes. Blotner,<sup>4</sup> in 1945, found that of 70 nondiabetic adults with illnesses causing prolonged physical inactivity, 63 had blood sugar findings indicative of decreased glucose tolerance. There has been evidence that tuberculous patients have a tendency toward decreased glucose tolerance although Kramer's study of 98 tuberculous patients<sup>5</sup> showed only 17 per cent with such a tendency.

In recent years a great deal of importance has been placed upon protein in the diet. This is especially true of the influence of protein on resistance to infection and repair of injured tissues. Cannon<sup>6</sup> in 1943, postulated that a large protein reserve was necessary to maintain proper antibody response and the phagocytic activity of mesenchymal cells. He showed that hypoproteinemic rabbits had markedly lessened ability to produce agglutinins. Madden and Whipple<sup>7</sup> observed in 1940 that blood protein levels directly reflected tissue protein stores. Krebs<sup>8</sup> in 1946, carefully studied the antibody response in a girl with a low total blood protein level and an extremely low gamma globulin fraction. After a full course of immunization with typhoid vaccine, she failed to develop any antibody. The maintenance of high protein levels has

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\*From the Thoracic Diseases Service, Birmingham Veterans Administration Hospital, Van Nuys, California. Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

been long recognized as necessary to rapid healing of surgical wounds and ulcers Lund,<sup>9</sup> in 1945, also observed delayed gastric emptying time and edema of surgical stomata in hypoproteinemic patients

Vitamin studies in relation to tuberculosis have been particularly concerned with vitamins A and C Goetz, et al,<sup>10</sup> in a study of 275 tuberculous and nontuberculous patients found vitamin A deficiencies particularly in the tuberculous group, increasing in degree with the severity of the tuberculous process They also noted a marked vitamin C deficiency in the tuberculous group Sweaney and his associates,<sup>11</sup> in 1941, also noted an unaccountable exhaustion of vitamin C in tuberculous patients, increasing with the severity of the disease Menkin, et al,<sup>12</sup> in 1934, had demonstrated an apparent action of vitamin C to stimulate fibroblasts to increase connective tissue formation

To investigate the relationship of appetite to blood sugar levels, we selected 55 patients with far advanced pulmonary tuberculosis All of these had progressive disease with cavitation and all except four had bilateral involvement All had shown persistent loss of weight for two to eight months prior to this study Forty-nine of these patients stated that, although their appetites for breakfast were fairly good, they had little or no appetite for the succeeding two meals which ordinarily are served at four hour intervals

Six hour glucose tolerance test curves were observed in 47 of these 55 patients Thirty-seven, or 77 per cent showed definitely abnormal curves and only seven, or 15 per cent had normal tolerance curves The abnormal curves fell into two distinct types Twenty-six, or 55 per cent, demonstrated a sharp blood glucose rise in the first half hour with a slow decline, not returning to the base line before three hours, this was designated as a Type I curve Ten, or 22 per cent, showed a sharp rise continuing beyond the first hour, falling slowly and not returning to the base line until four hours after ingestion of the glucose, this curve was designated Type II Significantly, all ten patients demonstrating Type II curves were extremely ill, four are now dead and four are terminal Graphic representation of these glucose tolerance curves are shown in figure one

On the premise that the poor appetite of these patients might be due to a hyperglycemia prolonged into the next meal period, a two meal diet was devised, composed of an unusually large breakfast and a supper eight hours later, interrupted only by a light noon supplemental feeding The diet had values of approximately 3400 calories, protein 160 grams, fat 77 grams, carbohydrate 560 grams Our normal hospital diet has approximately the same caloric value, but definitely lower value for protein

Although these patients were for the most part on a high vitamin regimen, this experimental diet provided daily supplements of 5000 units A, B and D with 500 mg of ascorbic acid to obviate the effect of any deficiency factor. Breakfast and supper were approximately the same in nutritional values, with each consisting of from 220 to 250 grams of carbohydrate, 60 grams of protein, and 30 grams of fat. Two hundred and fifty to 400 calories were allotted to a mid-day and an evening supplement consisting of an egg nog formula and cookies. Each patient accepting this diet was provided an intake chart with instructions to chart accurately the proportion of each food item rejected daily. After a short time on the diet it was found that the low fat content decreased the palatability of the diet, which was then changed, raising the fat content to 150 grams at the expense of carbohydrate which was reduced to 350 to 370 grams.

Only 24 of the 55 studied as to glucose tolerance would accept the rigid limitations of this diet and keep an intake chart accurately enough to study. These 24 patients recorded on an intake chart the exact proportions of each dietary item taken. Their weight trends for two months prior to the diet and for two months on the diet were tabulated, as well as toxicity evaluations, blood studies, blood protein studies and liver function tests. Nineteen of these patients had marked toxicity evidenced by fever and increased erythrocyte sedimentation rates. Eighteen had compli-

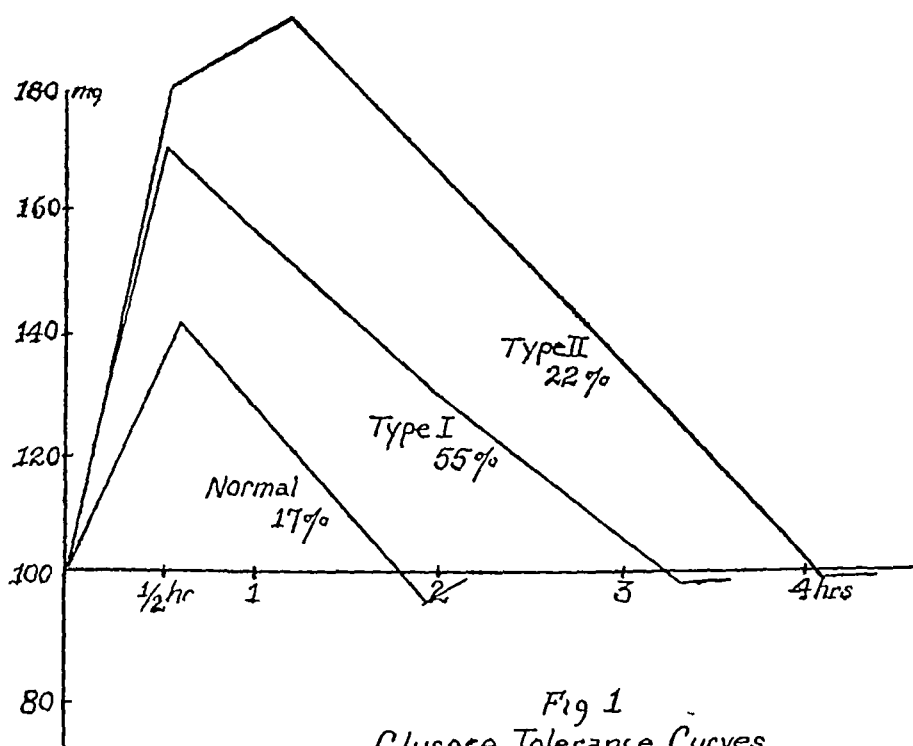


Fig 1  
Glucose Tolerance Curves



over, only five showed any loss of weight and of 22 periods studied in patients with an intake of less than 80 per cent, 17 showed loss of weight. At 80 per cent intake, the gains and losses were equal. The elements of food rejected amounted in carbohydrate, protein and fat to approximately the same ratio as in the total diet.

A careful computation and analysis of their intake charts disclosed that these 24 patients had averaged over the two months period on the diet, a daily intake of carbohydrates 297 grams, proteins 119 grams, and fats 120 grams. This natural selection corresponded very closely with 80 per cent of the prescribed diet, i.e., carbohydrates 297 grams, protein 128 grams, fats 120 grams. Since the average weight of these patients was 132 pounds, it might be said that the dietary components necessary to reverse the weight loss trend of this group was, per kilogram of body weight, carbohydrates 50 grams, proteins 20 grams, fats 20 grams. It was also noted that in selecting two week periods during which the patients had fever averaging over 99.6 degrees F, 12 of these with food intake of 80 per cent and over showed weight gain in ten periods and loss in two, one of which was associated with diarrhea. Again, in two febrile periods of two weeks duration with food intake of 80 per cent there was found neither gain nor loss of weight.

Blood protein studies before and after this high protein diet showed no essential change from those of our controls. Total blood proteins remained slightly above the low normal levels. These patients showed generally an increase in globulin and a decrease in albumin fractions, reflecting the general trend of our far advanced tuberculous patients. These fractions approached equality, but never a reversal. We could not determine that our diet influenced this trend. The hemoglobin level showed a general increase with 14 patients showing increase of hemoglobin, five decreased levels, and five maintaining a normal level before and after the diet. Nine patients showing increased hemoglobin levels were in the higher food intake group compared with five in the group with intake of under 80 per cent. Most of the patients expectorated large quantities of sputum. In order to determine if this represented a significant loss of protein, five patients were selected who produced copious amounts of mucopurulent sputa. The largest amount of protein found in any 24 hour accumulation was 11 gram.

### SUMMARY

1) Decreased glucose tolerance was found in 37 of 47 patients with far advanced pulmonary tuberculosis. These patients all demonstrated poor appetites except for the breakfast meal. The

glucose tolerance curves showed prolongation of hyperglycemic levels beyond the third and fourth hours following ingestion of the glucose. On the premise that their poor appetites for the succeeding meals were due to prolonged hyperglycemia a two meal high protein diet was devised with 8 hours between meals.

2) Careful weight, food intake, and blood protein studies were made on 24 far advanced tuberculous patients on this diet. These patients showed a weight reversal from a previous average loss of 25 pounds per man two months prior to the diet to an average gain of 19 pounds per man during two months on the diet. A critical level of food intake for weight maintenance in this group was found to be 2700 calories divided into 297 grams carbohydrates, 128 grams protein and 120 grams fat. Above this level the great majority of these patients gained weight regardless of fever or other evidence of toxicity.

3) Hemoglobin levels of patients on this diet showed a general increase over the levels 2 months prior to the diet. Total blood proteins showed no essential change over those of the controls. Protein loss in the sputum was found to be negligible.

### RESUMEN

1) En 37 de 47 pacientes con tuberculosis pulmonar avanzada se encontró disminución de la tolerancia a la glucosa. Todos estos pacientes tenían mal apetito excepto en el desayuno. Las curvas de la tolerancia a la glucosa revelaron prolongación de los niveles hiperglicémicos por más de tres o cuatro horas después de la ingestión de la glucosa. Sentando como premisa que sus malos apetitos en las comidas subsiguientes se debían a la prolongada hiperglicemia, se ideó una dieta alta en proteínas que consistió de dos comidas separadas por ocho horas.

2) Se llevaron a cabo estudios cuidadosos del peso, la ingestión de los alimentos y las proteínas de la sangre en 24 tuberculosos muy avanzados sometidos a esta dieta. Estos pacientes revelaron una reversión del peso de un promedio anterior de pérdida de 25 libras por hombre, dos meses antes de comenzar la dieta, a un promedio de aumento de 19 libras por hombre durante los dos meses de dieta. Se encontró que el nivel crítico de ingestión de alimentos necesario para mantener el peso en este grupo fue de 2,700 calorías, divididas en 297 gramos de carbohidratos, 128 gramos de proteínas y 120 gramos de grasas. Con dietas más altas de este nivel la gran mayoría de esos pacientes ganaron en peso, a pesar de fiebre u otros signos de toxicidad.

3) Aumentaron los niveles de la hemoglobina en los pacientes en esta dieta, comparados con los niveles de dos meses antes de la dieta. El total de las proteínas de la sangre, comparado con el



de los testigos, no mostró alteración significativa. Se encontró que fue menos apreciable la pérdida de proteína en el esputo.

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## Cervical Vagus—Sympathetic Block in Pulmonary Embolism\*

WILLIAM A WERNER, MD and  
LEWIS H FERGUSON, JR, MD  
St Louis, Missouri

The consequences of pulmonary embolism are at best poorly understood. It has long been evident that factors other than the mere interruption of a vessel supplying a lung segment are operating to produce the clinical picture of pulmonary embolism.

Varying importance has been attached to the sudden strain embolism may impose on the right side of the heart. The degree of mechanical obstruction in the pulmonary circulation is certainly a major element in some cases. This mechanical stress is modified by reflexes arising in the pulmonary vascular bed, although the presence of a pulmono-coronary reflex is difficult to prove.

James Currens<sup>1</sup> states that any actual coronary insufficiency is best explained by shock and a rise in the pressure in the right heart chambers. The venous drainage and Thebesian vessels empty mainly into the right side and are impeded by increased right heart pressure. If the cardiac function should be compromised by pre-existing disease, a sizeable pulmonary obstruction, or relative coronary insufficiency, the development of an acute cor pulmonale would easily explain the picture.

However, often the symptoms of shock and collapse may predominate even with small emboli,<sup>2</sup> when neither electrocardiogram nor postmortem examination reveals evidence of cor pulmonale. A major role of reflex vaso and bronchospasm is postulated in such instances of embolism, but this role is difficult to evaluate at this time. The work of Boyer and Curry<sup>3</sup> indicates that in dogs pulmonary embolism causes reflex bronchoconstriction of a transient nature and some doubt is cast upon its practical importance. Their observations also suggest that reflex bronchospasm may be dependent on a pressure rise in the pulmonary artery and the right side of the heart. Megebow, Katz, and Feinstein<sup>4</sup> gathered evidence to show that the acceleration in respiration was also due to this pressure increase.

deTakats, Fenn, and Jenkinson<sup>5</sup> cite evidence to show that reflex bronchospasm with increased bronchial secretion occurs in the

\*From St. John's Hospital, St. Louis, Missouri.

experimental animal They believe that these two factors produce an atelectasis which accounts for the radiologic picture of infarction and perhaps many of the symptoms of embolism

Whatever the eventual role assigned to each of these elements, it remains that our present rationale of therapy is directed at relief of the reflex spasms as well as supporting the circulation and the respiratory center Oxygen, papaverine, and ephedrine seem to have met these requirements reasonably well

Villaret, Justin-Besancon, and Bardin,<sup>6</sup> investigating pulmonary embolism, found that vagotomy along with ephedrine and atropine all acted favorably in increasing dog's tolerance to repeated emboli and in delaying embolic death The opposite effect was obtained by section of the cervical sympathetic nerves The reflex inhibition of the sympathetic system was responsible for hastening sudden death, but there may also be other factors acting, since the rate of discharge from the respiratory center is slowed to a less extent in animals with pulmonary embolism than in normal animals Thus deterioration may be postponed by the lessened oxygen requirements of the center Also, the purity of the sympathetic and vagus trunks has become ever less impressive Katz,<sup>7</sup> for example, now has evidence that the vagi are coronary dilators, not constrictors, and the sympathetic nerves cause both a vasodilatation and vasoconstriction of the coronaries when the effect on cardiac work and metabolism is not considered

Elimination of both vagal and sympathetic influence was attempted by Skvortsov<sup>8</sup> in a variety of war casualties such as open pneumothorax and lesions of the upper extremities A vagus-sympathetic block in the neck was performed with procaine infiltration on men who were in a state of shock In the cases of open pneumothorax, pain and dyspnea disappeared in about 91 per cent, the cough reflex disappeared, and the manifestations of shock gradually vanished in the course of one to two hours A similar procedure was carried out in the following instance

#### CASE REPORT

Mrs E L H, a 41 year old housewife, entered the hospital October 25, 1947 complaining of pain in abdomen with nausea and vomiting for about seven weeks Physical examination revealed marked tenderness over the right upper quadrant Her daily temperature reached 103 degrees RBC, 29, Hb, 85, WBC, 8650 Attempts to visualize the gall bladder radiologically were unsuccessful The patient did not respond to chemotherapy A diagnosis of ruptured gall bladder with abscess formation was made She was prepared for surgery and operated on November 10, 1947

She was found to have a ruptured gastric ulcer with a grapefruit sized abscess inferior to the gall bladder Her postoperative course remained febrile and on December 5, 1947 she developed phlebitis of the right leg



## RESUMEN

En la producción del cuadro clínico de la embolia pulmonar, se les ha atribuido variable importancia a las alteraciones de la presión de la circulación pulmonar, al vasoespasmo y broncoespasmo reflejos y a la producción refleja de la atelectasia pulmonar. En los perros, la atropina y la vagotomía ayudan a aumentar la tolerancia a la embolia pulmonar. Skvortsov empleó con buen éxito un bloqueo vago-simpático cervical con procaina en una variedad de heridos de guerra en los que el choque complicaba a heridas del tórax y de las extremidades superiores. Se presenta un caso de embolia pulmonar seguida de choque grave en el que se empleó con buen éxito el bloqueo vago-simpático cervical.

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# Fifteenth Annual Meeting

## AMERICAN COLLEGE OF CHEST PHYSICIANS

As this issue of the journal goes to press the *Fifteenth Annual Meeting* of the College will be in session at the Ambassador Hotel, Atlantic City. Advance reservations indicate that there will be a record attendance at this meeting. Subscriptions for the Round Table Luncheon Meetings have been received at the Executive Offices in such numbers as to assure a capacity attendance at each of the luncheons. Arrangements have been made for meetings of the Board of Regents, Board of Governors, Executive Council, and all other councils and committees of the College.

A very interesting scientific program has been arranged by the Committee on Scientific Program and papers on a great variety of subjects will be presented by outstanding authorities in their fields. New features in the program will include critical reviews in chemotherapy, respiratory physiology, roentgenology, medical aspects of diseases of the chest and thoracic surgery, and a motion picture session devoted to diseases of the chest. One afternoon session will be devoted to an x-ray conference. Reports of the meeting will be published in future issues of *Diseases of the Chest*.

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## College Chapter News

### FLORIDA CHAPTER

At the first meeting of the Florida Chapter, held in Belleair on April 10, the following officers were elected for the chapter:

E. C. Brunner, M.D., Miami, President  
Arnold S. Anderson, M.D., St. Petersburg, Vice-President  
Howard K. Edwards, M.D., Miami, Secretary-Treasurer

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### NEW ENGLAND STATES CHAPTER

The New England States Chapter held its annual meeting at the Deaconess Hospital, Boston, Massachusetts, on May 11. Dr. Walter L. Phillips of Capetown, South Africa, was the guest speaker; he spoke on "Tuberculosis Problems in South Africa" and also presented a very interesting film in which a hydatid cyst of the lung was treated by means of a lobectomy. The newly elected officers of the chapter are:

Moses J. Stone, M.D., Boston, Massachusetts, President  
Hubert A. Boyle, M.D., New Bedford, Massachusetts, Vice-President  
John B. Andosca, M.D., Mattapan, Massachusetts, Secy.-Treas.

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### NEW JERSEY CHAPTER

At the annual meeting of the New Jersey Chapter held in Atlantic City on April 28, the following officers were elected for the ensuing year:

Homer H. Cherry, M.D., Paterson, President  
Joseph A. Smith, M.D., Glen Gardner, First Vice-President  
Juan R. Herradora, M.D., Jersey City, Second Vice-President  
Benjamin P. Potter, M.D., Jersey City, Secretary-Treasurer

## NEW YORK STATE CHAPTER

At the annual meeting of the New York State Chapter of the College, held in Buffalo on May 5, the following officers were elected

Roger A Hemphill, M D , Mt Morris, President  
Joseph J Witt, M D , Utica, First Vice-President  
David Ulmar, M D , New York, Second Vice-President  
Donald R McKay, M D , Buffalo, Secretary-Treasurer

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## OHIO CHAPTER

The Ohio Chapter held its annual meeting at the Nell House, Columbus, on April 20 at which time the following officers were elected for the ensuing year

Karl P Klassen, M D , Columbus, President  
Lynne E Baker, M D , Dayton, Vice-President  
E F Conlogue, M D , Dayton, Secretary-Treasurer

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## POTOMAC CHAPTER

At the annual meeting of the Potomac Chapter, held in Baltimore on April 27, the following officers were elected for the year 1949-1950

Edgar W Davis, M D , Washington, D C , President  
Hugh G Whitehead, M D , Baltimore, Maryland, Vice-President  
Milton B Kress, M D , Towson, Maryland, Secretary-Treasurer

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## ROCKY MOUNTAIN CHAPTER

Dr Ralph G Rigby, Salt Lake City, Utah, President of the Rocky Mountain Chapter, has announced the following committee appointments

*Program Committee*

H M Van der Schouw, M D , Wheatridge, Colorado, Chairman  
John B Grow, M D , Denver, Colorado  
Carl W Tempel, M D , Denver, Colorado  
W R Rumel, M D , Salt Lake City, Utah

*Publicity Committee*

John S Bouslog, M D , Denver, Colorado, Chairman  
Fred Harper, M D , Denver, Colorado  
Carl H Gellenthien, M D , Valmora, New Mexico  
Robert C Cook, M D , Ft Logan, Colorado

*General Arrangements Committee*

Arnold Minnig, M D , Denver, Colorado, Chairman  
B T McMahon, M D , Denver, Colorado  
Lorenz W Frank, M D , Denver, Colorado  
James H Forsee, M D , Denver, Colorado



### TEXAS CHAPTER

The following officers were elected at the annual meeting of the Texas Chapter held in Houston on May 2nd

Jesse B White, M D , Amarillo, President  
David McCullough, M D , Kerrville, First Vice-President  
Charles J Koerth, M D , San Antonio, Second Vice-President  
Henry R Hoskins, M D , San Antonio, Secretary-Treasurer

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### CALIFORNIA CHAPTER

At the annual meeting of the California Chapter of the College held in Los Angeles on May 8, the following officers were elected for the coming year

Lyman A Brewer, M D , Los Angeles, President  
Seymour M Farber, M D , San Francisco, Vice-President  
C Gerald Scarborough, M D , San Jose, Secretary-Treasurer

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### ANNUAL REPORT, SOUTH AFRICAN CHAPTER

The first Chapter of the American College of Chest Physicians in the Union of South Africa was organized on April 28, 1948 There are 25 members of the College in the Union of South Africa, with David P Marais, M D , as Regent The 16 members residing in the Southern States have formed the above Chapter with Theodore Schrire, M D , as Governor, and when a sufficient number of members of the College are enrolled in the Northern States, it is planned to charter a chapter for that district P J Kloppers, M D , is Governor for the Northern States

The early meetings of the Chapter were largely taken up by detailed discussions of the aims and objectives of the Chapter and it was the general opinion that the group should become interested in the problem of tuberculosis in South Africa, as well as to conduct scientific programs in chest diseases At one of the meetings, the various aspects of pleural effusion were discussed in a series of papers and a paper was also read on atelectasis One evening was devoted to the showing of films and other meetings were occupied by the presentation of brief clinical cases and records presented by members of the College

All of the meetings were well attended and the enthusiasm of the Fellows was equalled only by the high order of the scientific discussions

s/ H H Jacob, M D , F C C P , Secretary-Treasurer

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### CUBAN CHAPTER

On April 26th, at the Academy of Sciences, Havana, Cuba, the Cuban Chapter of the College presented a Round Table Conference on Pulmonary Abscess Antonio Navarrete, M D , Regent of the College, presided at the meeting and reported a large attendance Francisco J Menendez, M D , President of the Cuban Chapter of the College was one of the speakers Other speakers were Francisco Perez Carballas, M D , Pedro L Fariñas, M D , Rufino Moreno, M D , Orfilho Suarez de Bustamente, M D , and Rogelio Barata, M D

## PORTUGUESE CHAPTER ORGANIZED MARCH 27, 1949

On March 27, 1949, the organizational meeting of the Portuguese Chapter of the American College of Chest Physicians took place in Coimbra, Portugal. The following officers were elected:

Augusto Vas Serra, M D, Coimbra, President

Antonio S Araujo, M D, Porto, Vice-President

Lopo Cancellia, M D, Lisbon, Secretary-Treasurer

Lopo de Carvalho, M D, Governor of the College for Portugal stated that Coimbra was selected as the site for the first meeting in homage to the University of Coimbra, where the first school of medicine was established.

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## College News Notes

Dr E W Hayes, Monrovia, California, Past-President of the College, has been elected President of the California Tuberculosis and Health Association to succeed Dr Harry C Warren, San Francisco, Second Vice-President of the College.

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Dr Carl C Aven, Atlanta, Georgia, has been appointed Chairman of the Board of Governors of the College to complete the unexpired term of Dr Robert K Campbell of Springfield, Illinois, who has resigned the office because of illness. Dr Italo Volini, Chicago, Illinois, has been appointed to serve the unexpired term of Dr Campbell as Governor of the College for Illinois.

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Dr William C Voorsanger, San Francisco, California, received the annual award of the California Tuberculosis and Health Association for meritorious service in the field of tuberculosis control. The presentation was made by Dr R S Sundberg of San Diego, California.

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Dr Chevalier L Jackson, Philadelphia, Pennsylvania, has recently returned from Mexico City where he participated in a postgraduate course in bronchoesophagology.

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Dr Leon Unger, Chicago, Illinois, is leaving for a visit to Great Britain early this month.

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The Council of Tuberculosis Hospitals of the College held a meeting at the Congress Hotel, Chicago, on April 9th. The following members of the council attended the meeting: Dr R S Anderson, Erie, Pennsylvania, Chairman, Dr E W Custer, South Bend, Indiana, Dr Charles A Brasher, Mount Vernon, Missouri, Dr E F Conlogue, Dayton, Ohio, and Dr David F Loewen, Decatur, Illinois. The council will make a report of its activities at the annual meeting of the College.

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Dr Otto L Bettag has been appointed as medical superintendent and tuberculosis control officer of the Municipal Tuberculosis Sanitarium, Chicago, Illinois. Dr Bettag was formerly medical director of the Livingston County Tuberculosis Sanatorium in Pontiac, Illinois.

## Book Reviews

THE CHEST AND THE HEART, By J Arthur Myers and C A McKinlay  
Charles C Thomas, Publisher, Springfield, Illinois

J Arthur Myers did it again With the assistance of C A McKinlay he has compiled in two volumes 1800 pages of pertinent information on diseases of the chest Undoubtedly realizing the importance of heart problems in diseases of the chest, Dr Myers mobilized such cardiologists as Willhus, George Herrmann, Ralph Major and a number of other equally well known men to contribute on the heart It makes one feel happy to realize that chest specialists do not any longer concern themselves only with tuberculosis of the lungs

Myers and McKinlay compiled this two volume edition with the aid of sixty-one experienced specialists Scammon, Rasmussen, and Myers wrote respectively on the embryology, innervation and gross anatomy of the chest Maurice Visscher and Victor Lorber devoted thirty interesting pages to the physiology of respiration

Among the numerous topics discussed by Dr Myers himself, one may read on the diseases of the diaphragm, diseases of the mediastinum, diseases of the trachea, and bronchi, pulmonary abscess, syphilis, glanders and anthrax, pulmonary emphysema, inhalation of fumes, gases, and vapors, inhalation of dusts, air-borne infections, air conditioning, the tubercle bacillus, first infection type of tuberculosis, reinfection type of tuberculosis, treatment by intrapleural artificial pneumothorax, tuberculosis of the lymphatic system, tuberculosis case finding and finally veterinarian's contribution to control of tuberculosis

C A Stewart wrote on the normal chest in infancy and childhood Porter Vinson discussed diseases of the esophagus Kinsella took up chest injuries, while Simons and Stuart Harrington discussed respectively malignancies of the chest, and benign intrathoracic tumors

Harold S Diehl devotes 18 pages to an excellent discussion of all important phases of the common cold Hinshaw wrote two chapters on pulmonary edema and pulmonary embolism Adamson discussed pulmonary atelectasis, while Moorman took up cystic diseases of the lungs

Surgical features have been written up by Thomas J Kinsella and Richard Davison

Chapters on mycoses of the lungs were contributed by Henrici and Emmons, Towey, David T Smith, and Farness The chemistry of the tubercle bacillus was discussed by Long and Seibert The chapters on artificial pneumoperitoneum and tuberculosis of the abdomen were written by Edward H Hayes McKelvey wrote two chapters on gynecological tuberculosis and tuberculosis in obstetrics Bone and joint tuberculosis was covered by John H Moe Tuberculosis of the nervous system is written up by John E Skogland Francis M Walsh covered tuberculosis of the eye, and Michelson and Layman discussed tuberculosis of the skin Erythema nodosum was taken up by Wesley W Spink Epidemiologic phases of tuberculosis were covered in three chapters by Hilleboe and also Myers

The second section of the "Chest and the Heart" takes up about 400 pages jam packed with information about the heart

Part one takes up in one chapter the examination of the normal heart and blood vessels and in another chapter normal heart beat and the carotid sinus reflex, both chapters ably written by S Marx White The

chapter on venous pressure and circulation time is discussed by George N Aagaard The roentgenology of the heart is taken up by Ungerleider and Gubnei The physiologic and physical aspects of the electrocardiogram are discussed by Richard Ashman

Part two takes up congenital heart disease, cor pulmonale and diseases of the great vessels Sako writes on congenital heart disease, Willius discusses cor pulmonale, and Tuohy takes up the great vessels

Part three includes the heart in pregnancy, discussed by Jensen, cardio-vascular disturbances written by George Herrmann The chapter on cardiac arrhythmia is contributed by Peter Bohan, while the chapter on the heart in thyroid disease is considered by C A McKinlay

Four chapters are devoted in part four to infectious heart disease Hansen writes the chapter on rheumatic heart disease The chapters on pericarditis and valvular disease are taken up by Willius, while Ralph Major considers endocarditis in another chapter

Part five contains three chapters on hypertension and degenerative heart disease The chapter on hypertension is written by Page, while Nadler discusses hypertensive heart disease, and Barnes takes up coronary sclerosis

Part six takes up the prevention and treatment of heart disease in three chapters Glomset discusses the prevention of premature heart failure Hirschboeck writes on the treatment of heart failure, and Richard Davison takes up cardiac surgery

In an appendix of twenty pages Harry C Sweany ably discusses the pathogenesis of tuberculosis

The "chest and the heart" written and compiled by Myers and McKinlay with over sixty competent authors contributing on all phases of diseases of the chest which naturally includes the heart, the mediastinum, the chest wall and the diaphragm brings together in two volumes encyclopedic information regarding any and most all phases of diseases of the chest The literature on the various topics is brought down to 1946 and in many cases to 1947 The method of approach is both purely scientific and also practical from the view point of clinical application The illustrations and charts are very illuminating The combined author and subject index to which about 60 pages are devoted, makes "the chest and the heart" an indispensable reference book on diseases of the chest

This book is an anthology of the most recent information on problems involving the chest organs It is truly a ready reference book well adapted for the medical student, the general practitioner, as well as the specialist on diseases of the chest

M Joannides, M D

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TUBERCULOSIS (A Discussion of Phthisiogenesis, Immunology, Pathologic Physiology, Diagnosis, and Treatment), by Francis Marion Pottenger, A M, M D, L L D, F A C P, Emeritus Professor of Medicine, University of Southern California, the School of Medicine, Medical Director, the Pottenger Sanatorium and Clinic for Diseases of the Chest, Monrovia, California Published by The C V Mosby Company, St Louis, Missouri, 1948

Rarely does it fall to the lot of one man to bridge completely two generations of medicine Dr Pottenger is one of those men Although many changes have taken place in the handling of tuberculosis since the first two volume set on Pulmonary Tuberculosis was published, he

has adapted himself exceedingly well to the changes and has made a valuable contribution in the present volume

The author's own apology for devoting so much space to phthisiogenesis seems to this reviewer, unwarranted. The discussion is scholarly, accurate and pertinent. In the classical clinical fields the work is unsurpassed. The writing is clear, it is easy and actually pleasant to read, the text is concise, complete and generally correct—just what one would expect from a man of Dr. Pottenger's vast experience.

It would be expecting too much—in fact the impossible—however, to hope for one man to have everything perfect under the circumstances. Every one has his special interests that may be over-played and other useful ideas not sufficiently emphasized. In a minor degree, this text is no exception. For example, in a moderate sized text, it would seem that a little too much emphasis is placed on the problems of reflexes. There are probably few clinicians today who make use of anything but the elementary aspects of the "spasm" and "atrophy" of muscles overlying the diseased lung. Since most books are predominantly utilitarian, there would seem to be much academic discourse that could well have been left to larger treatises. Not that the discussion isn't interesting, scientific and even profound, but there are so many interfering factors arising within the chest, that the use of the reflex signs are limited, more than the text would lead one to believe.

The same points may be raised to the use of tuberculin in treatment. Tuberculin was used in treatment at the turn of the century and can still be used effectively by Dr. Pottenger and a few others in certain types of disease. But the same may be said of gold treatment, yet few texts mention the latter and the former should probably merely be mentioned today in passing. The temptation is great for a man with such a storehouse of knowledge to refrain from dilating on a method that he knows so well and knows how to use so well. Yet nothing can contradict the fact that the use of tuberculin in treatment of tuberculosis is *passee* and, that after all, the book is limited in space.

The "dilution-flotation" method of finding tubercle bacilli is another "favorite" that is mentioned to the exclusion of all other methods. Not that the method isn't good. It is. But most workers have found the method too time consuming for ordinary use and if a more laborious method *must* be used, bronchial aspiration surpasses all others, especially when the aspired material is cultured. The common methods should have been mentioned such as those advocated by the American Trudeau Society. This reviewer does not subscribe to the statement "that every student is familiar" with the "usual method of examining sputums." Under no circumstances is the finding of tubercle bacilli in either the early, the complicated, or the healing case, a matter for "students." Especially is that true with the culture method of diagnosis which the author has failed to mention.

The chapter on the x-ray could have recommended the use of lateral, oblique, lordotic positions as well as planographs and "spot" pictures. In the complications of the disease, genito-urinary, bone, joint, adrenal, milary, meningeal, cold abscesses and other disease localizations might have been mentioned to advantage. The subjects the author does discuss, such as hemorrhage, enteritis, pleurisy, etc., however, are classics. The chapter on compression therapy only gives one small paragraph to pneumoperitoneum and none at all to extrapleural pneumothorax.

and segmental resection While extrapleural pneumothorax is unquestionably controversial, yet there are a sufficient number of advocates of the method to warrant mention On Page 557, Figure 99 would hardly be considered an "ideal" pneumothorax although many such cases have healed in the past Most workers today would re-expand that type and do another form of collapse The use of the bronchoscope has also been omitted together with the information obtained by its use Finally, it doesn't seem to be unreasonable to expect that a book published in 1948 on tuberculosis would go into more detail on streptomycin treatment of tuberculosis and its complications

Most of these points raised perhaps appear, and many probably are, out of proportion to their importance They are nevertheless objections that most workers today will agree with In this "smoke screen," however, the sterling worth of the chapters on phthisiogenesis, physical diagnosis, childhood tuberculosis, classical treatment, and other gems throughout the text should not be lost sight of The illustrations are generally well chosen and of excellent quality The binding and paper are of the best

No one today in chest disease work can afford to be without this most valuable contribution to tuberculosis literature

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#### MEETING ON ANTHRACOSILICOSIS

The members of the College in West Virginia presented a program on "Anthracosilicosis" at the Daniel Boone Hotel, Charleston, on May 19 The speakers were Drs Burgess Gordon, Peter A Theodos, Hurley L Motley and Leonard P Lang, all members of the staff of the Jefferson Medical College Hospital, Philadelphia, who have been making a study of anthracosilicosis, especially among anthracite miners

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#### BRITISH TUBERCULOSIS ASSOCIATION MEETING

Dr William Odgen, Regent of the College for Canada, addressed the British Tuberculosis Association at its annual conference held in Cambridge from April 6th to April 9th of this year The title of his paper was "Twenty Years Observation on the Development of Pre-Clinical and Clinical Tuberculosis" His presentation was based on clinical material published as a symposium in "Diseases of the Chest" in July-August 1946, under the title "Foreseeing and Forestalling Tuberculosis"

It is interesting to note that three other Fellows made important contributions to the British Tuberculosis Association program, Dr Irving Sarot of New York on resection for pulmonary tuberculosis with special reference to extrapleural resections and pleurectomy, Dr J M Lemoine, of Paris on atelectasis and Dr R R Trail who welcomed the Association and its guests to Papworth Village Settlement

Dr Joseph Lee of Hamilton, who is in England on an exchange arrangement, sponsored by the British National Association for the Prevention of Tuberculosis and who is attached to Clare Hall Sanatorium, Middlesex, also attended the meeting

It might be added that all five Fellows of the College were able to meet informally at the University Arms Cambridge, and indulge in a pleasant discussion of certain matters of mutual interest

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#### NEW OFFICERS OF AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION

At the annual meeting of the American Broncho-Esophagological Association held in Chicago, Illinois, on April 18 and 19, the following officers were elected

LeRoy A Schall, M D, Boston Massachusetts President  
Edwin N Broyles, M D, Baltimore, Maryland, Secretary

## Obituaries

### BURTON W RHUBERRY

1914-1948

Dr Burton W Rhuberry was born on May 2, 1914 in Detroit, Michigan. He was a graduate of the American High School, Buenos Aires, Argentina, and received his medical degree from Northwestern University. His internship was served at Grace Hospital, Detroit, and he later became resident in thoracic surgery at the Detroit Tuberculosis Sanatorium. At the time of Dr Rhuberry's death he was resident physician at the Leland Sanatorium. He was a Fellow of the American College of Chest Physicians, a member of the Wayne County Medical Society, the Michigan State Medical Society, the American Medical Association, the Phi Chi Fraternity and the Kismet Lodge FM. He is survived by his wife Dorothea and his daughter Gail Ann.

Willard B. Howes, M.D., Governor for Michigan

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### ROBERT OSGOOD BROWN

1890-1949

The untimely death of Robert Osgood Brown, M.D., F.C.C.P., on February 1, 1949, is a tragic loss to his professional colleagues and his many friends.

Dr Brown was born February 13, 1890 in Chicago, Illinois. He received his B.S. degree from the University of Chicago in 1912 and was graduated from Rush Medical College in June, 1914, interning at Cook County Hospital, Chicago until June, 1916. He was an officer in the National Guard and served with the Pershing Expedition on the Mexican Border in 1916. He entered the practice of medicine in Santa Fe, New Mexico in 1916, specializing in internal medicine and diseases of the chest.

He was a Fellow of the American College of Chest Physicians, serving as Governor for New Mexico since 1946. He was also a Fellow of the A.M.A. and of the American College of Physicians, a member of the American Heart Association, American Trudeau Society and the New Mexico Clinical Society.

Dr Brown was prominent in New Mexico both in medical and in civic affairs. He was formerly Associate Medical Director of Sunmount Sanatorium, staff member of St. Vincent Sanatorium and Hospital, founder and member of the Board of Directors of The Santa Fe Clinic and Foundation for Research and Treatment of Cancer, Santa Fe. He was actively interested in Public Health and Welfare work in New Mexico, having served as Chairman of the New Mexico Public Welfare Board, Medical Consultant to the New Mexico Department of Public Welfare, and served for years as Chairman of the Legislative Committee of the State Medical Society. He was Past President of the New Mexico Medical Society, the New Mexico Tuberculosis Association, and was President of the Santa Fe County Tuberculosis Association at the time of his death.

He enjoyed an extensive and active practice. The community, his patients and his host of medical friends throughout the Southwest mourn his untimely death. We have lost a great and good friend and Doctor.

Carl H. Gellenthien, M.D., Regent

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